A COMPARATIVE STUDY OF INTRATHECAL DEXMEDETOMIDINE AND BUPRENORPHINE AS ADJUVANT TO BUPIVACAINE IN SPINAL ANAESTHESIA

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

DEPARTMENT OF ANAESTHESIOLOGY

THANJAVUR MEDICAL COLLEGE

THANJAVUR – 613004.

MARCH 2015

CERTIFICATE

This is to certify that the dissertation entitled, "A Comparative Study Of Intrathecal Dexmedetomidine And Buprenorphine As Adjuvant To Bupivacaine In Spinal Anaesthesia", submitted by **Dr.M.A.MOHAMED THAIYUB KHAN** in partial fulfilment for the award of the degree of **Doctor of Medicine in Anaesthesiology** by the Tamilnadu Dr.M.G.R. Medical University, Chennai is a bonafide record of the work done by him in the Department of Anaesthesiology, Government Thanjavur medical College, during the academic year 2012-2015.

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DECLARATION

I, **Dr.M.A.MOHAMED THAIYUB KHAN**, solemnly declare that the dissertation titled "A Comparative Study Of Intrathecal Dexmedetomidine And Buprenorphine As Adjuvant To Bupivacaine In Spinal Anaesthesia", is a bonafide work done by me at Thanjavur Medical College Hospital, Thanjavur, during 2012-2015.

The dissertation is submitted to **"The Tamilnadu Dr. M.G.R. Medical University, Chennai",** Tamilnadu as a partial fulfillment for the requirement of **M.D** Degree examinations – Branch -X (Anaesthesiology) to be held in April 2015.

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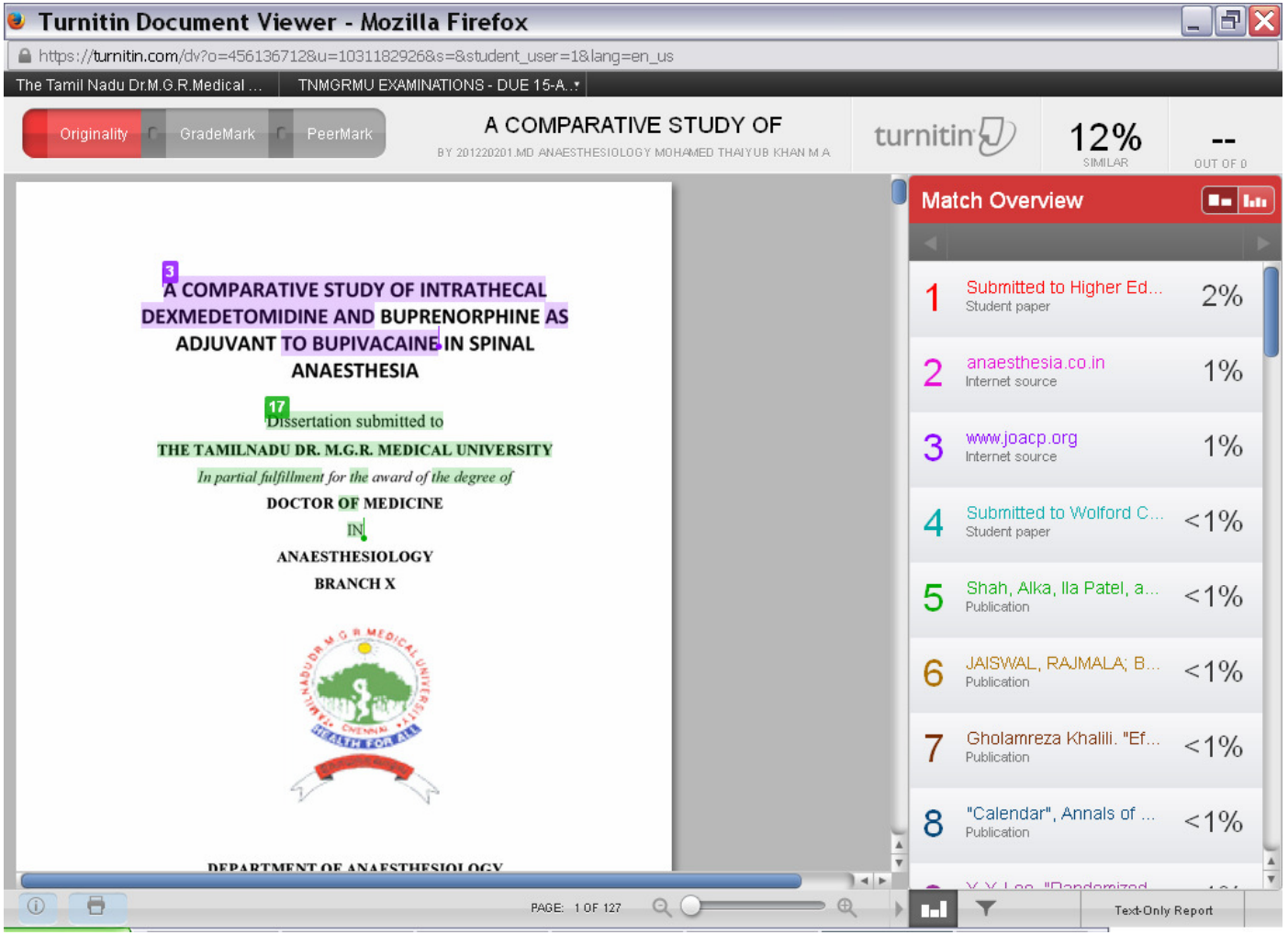
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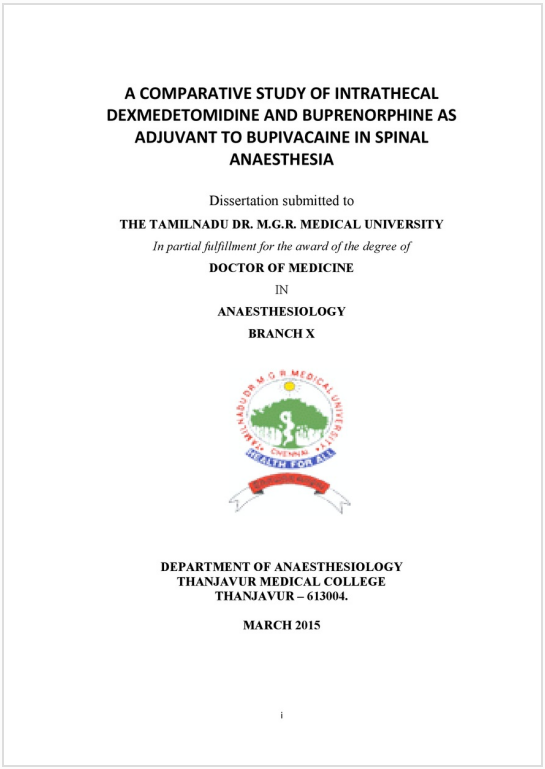

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A COMPARATIVE STUDY OF INTRATHECAL DEXMEDETOMIDINE AND BUPRENORPHINE AS ADJUVANT TO BUPIVACAINE IN SPINAL ANAESTHESIA

submitted by Dr. M.A. MOHAMED THAIYUB KHAN ..... of

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was approved by the Ethical Committee.

Thanjavur

Dated : .....

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CONTENTS

ABSTRACT

BACKGROUND:

The supplementation of local anaesthetics with adjuvants to improve the efficacy of subarachnoid block has been recognised since long. The most preferred drug has been opioids, but newer drugs like dexmedetomidine has also been introduced and investigated as an effective adjuvant.

AIM:

This study was conducted to evaluate and compare the characteristics of subarachnoid blockade, hemodynamic stability and adverse effects of intrathecal buprenorphine and intrathecal dexmedetomidine as an adjuvant to 0.5% hyperbaric bupivacaine for lower abdominal surgeries.

MATERIALS AND METHODS:

The present study included 60 patients aged between 18-60 years classified as American Society of Anaesthesiologists (ASA) Physical Status (PS) I/II scheduled for elective lower abdominal surgeries. The patients were randomly allotted into two groups namely Group BB and Group BD of 30 each. Patients in Group BB received 75µg of buprenorphine with 0.5% bupivacaine 15 mg intrathecally.Patients in Group BD received 5µg of dexmedetomidine with 0.5% bupivacaine 15 mg intrathecally. The onset time to peak sensory level, motor

block, sedation, Haemodynamic variables, duration of motor block, analgesia and any adverse effects were noted.

RESULT

There was no significant difference between groups regarding demographic characteristics and type of surgery. The motor, sensory blockade and time of rescue analgesia were significantly prolonged in Group BD compared to GroupBB. The sedation level was higher in Group BD compared to GroupBB. There was no significant difference in haemodynamic variables although GroupBB had lower Heart Rate (HR) than Group BD.

CONCLUSION:

Intrathecal dexmedetomidine when compared to intrathecal buprenorphine causes prolonged anaesthesia, analgesia with better degree of sedation and reduced need of rescue analgesics.

KEYWORDS:

Buprenorphine; Lower abdominal surgery; α–2 adrenergic agonist

INTRODUCTION

"It is the duty of the anesthesiologist to study the well being of the patient as well as the convenience of the surgeon"

-Ralph Waters

The International Association for the study of pain(IASP) defined pain as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage"[1].

Spinal anaesthesia was first performed by August Bier on 16th August 1898 when he injected 3 ml of 0.5% Cocaine intrathecally. It is a simple technique which has many advantages over epidural anaesthesia. In addition, correct placement of the needle in the subarachnoid space is confirmed by a clearly defined end point (appearance of CSF).

Spinal anaesthesia with local anaesthetic agents is extensively used for lower abdominal surgeries. It provides the excellent pain relief as compared to intravenous or epidural route.

There are many advantages for spinal anaesthesia over general anaesthesia which makes it the anaesthesia of choice in current surgical practice. Many clinical studies support the fact that Postoperative morbidity and mortality may be reduced when neuraxial blockade is used either alone or

in combination with general anaesthesia. Since it decreases the stay, it is cost effective for both patient and hospital. It is suitable for patients with respiratory diseases and helps in preventing intubation related problem like laryngospasm. It is also helpful in maintaining the airway patency and reduced blood loss.

Early return of gastro intestinal function following surgery can be considered as an added advantage. Other advantage may be reduced hypercoagulable state associated with surgery, increased tissue blood flow due to sympathectomy, decreased splinting which improves oxygenation, enhanced peristalsis, and reduced stress response to surgery due to suppression of neuroendocrine system [2].

Apart from the theoretical risk of infection to the brain, difficulty in finding the space in old age and bony abnormalities can pose a challenge to the anesthesiologist. The serious complication associated with spinal anaesthesia includes bradycardia, hypotension, prolonged motor block and high spinal [3]. It is related to the sympatholytic effect of local anaesthetic agents.

If the level of the block is higher, the sympatholytic effect will be more and leads to more serious complications. Though these effects cannot be abolished completely, they can be considerably minimized by using either low dose or low concentration of local anaesthetics. One of the main disadvantages

is the limited duration of block achieved with local anaesthetics. To overcome this, various adjuvants have been tried and used successfully.

This addition of adjuvant has further expanded the advantage of regional anaesthesia like

i) Rapid onset of action

ii) Reduces the local anaesthetic requirements

iii) Reduces the risk of local anaesthetic toxicity

iv) Prolongs the sensory block

v) Reduces the duration of motor block

vi) Improves the analgesic quality

vii) Improves the hemodynamic stability

viii) Inhibition of tourniquet pain

ix) Improved and prolonged duration of postoperative analgesia.

Opioids are the time honoured drugs which have been used for this purpose. Morphine was the first opioid used intrathecally in 1979, followed by other opioids [4 5 6]. Buprenorphine is a centrally acting lipid soluble analogue of alkaloid thebaine. It exhibits analgesic property both at spinal and supraspinal

levels [7]. It has been used for various surgeries at different doses for the past few decades. It has consistently proven to prolong the duration of anaesthesia[8 9 10] . At higher doses, it causes pruritus, drowsiness, nausea and vomiting [11].

Dexmedetomidine is a specific α-2 adrenergic agonist[12]. It has been extensively used as premedicant, for sedation in the Intensive Care Unit and for awake fibreoptic intubation [12 13]. It was first used intrathecally in humans for transurethral resection of prostate [14]. It prolongs both sensory and motor block and has nociceptive action for both visceral and somatic pain. It is being evaluated now as a potential adjuvant to local anaesthetic agents.

This research is designed to study the efficacy of such combination in our setup and compare the results with the previous studies done at other institutions.

AIM OF THE STUDY

To evaluate and compare the following factors in two groups – intrathecal dexmedetomidine and intrathecal buprenorphine as an adjuvant to 0.5% hyperbaric bupivacaine for lower abdominal surgeries, with respect to:

1. Sensory and motor blockade – Onset and duration.

2. Haemodynamic changes

3. Adverse effects

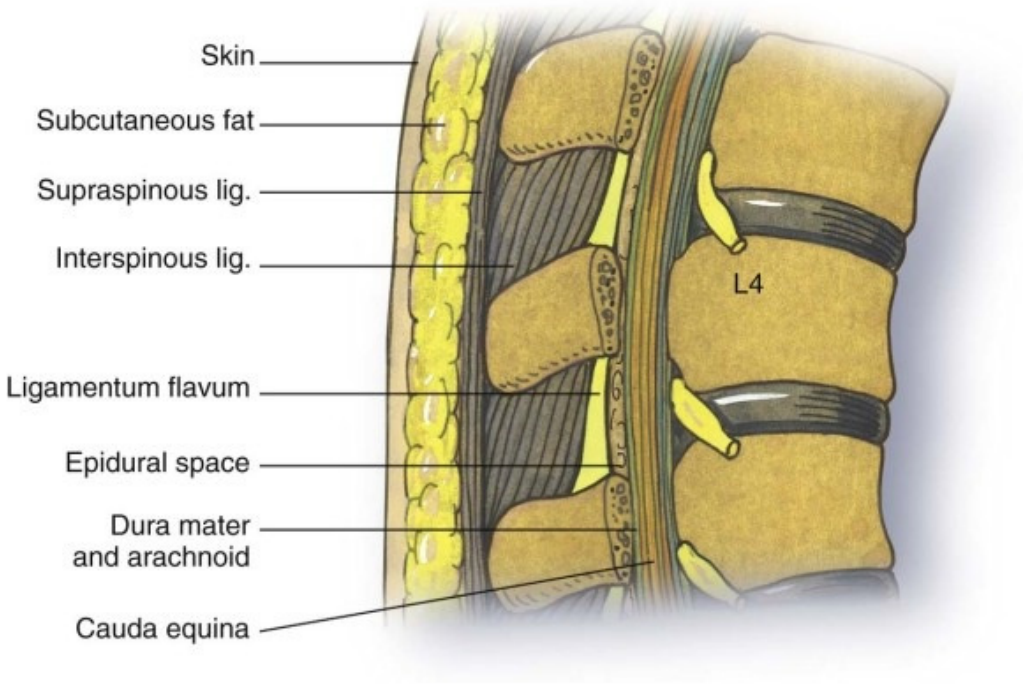
ANATOMY

Spinal anaesthesia results in sympathetic blockade, sensory analgesia or anaesthesia and motor blockade. It depends on the dose, concentration or volume of local anaesthetic injected into the subarachnoid space.

The vertebral canal extends from the foramen magnum to the sacral hiatus. There are seven cervical, twelve thoracic and five lumbar vertebrae. The sacrum comprises five and the coccyx four fused segments. The adult spine presents four curvatures: those of the cervical and lumbar zones are convex forwards (lordosis), whereas those of the thoracic and sacral regions are concave forwards (kyphosis).

The former are postural, while the latter are produced by the actual configuration of the bones themselves. The vertebrae are held together by a series of overlapping ligaments[15 16] namely

- Anterior longitudinal ligament
- Pterior longitudinal ligament
- Ligamentum flavum
- Interspinous ligament
- Supraspinous ligament
- Intervertebral discs.



There are certain common palpable landmarks that may correspond to particular level, including the most prominent spinous process which usually corresponds to the seventh cervical vertebra. The inferior angle of scapula usually corresponds to the seventh thoracic vertebra. Tuffier line, the line connecting the two iliac crests almost crosses the vertebral column at the level of L4-L5 intervertebral space.

The intervertebral canal consists of:

1. Roots of spinal nerves
2. Spinal membrane with the spinal cord and cerebrospinal fluid
3. Vessels, fat and areolar tissue.

The spinal cord is the continuation of medulla oblongata and it ends below in conus medullaris from which filum terminale descends vertically as cauda equina. The extent of the spinal cord is from the upper border of atlas to the lower border of first lumbar vertebra in adults. The spinal cord extends till the upper border of second lumbar vertebra and still lower in infants.

The coverings of spinal cord from outside to inside are

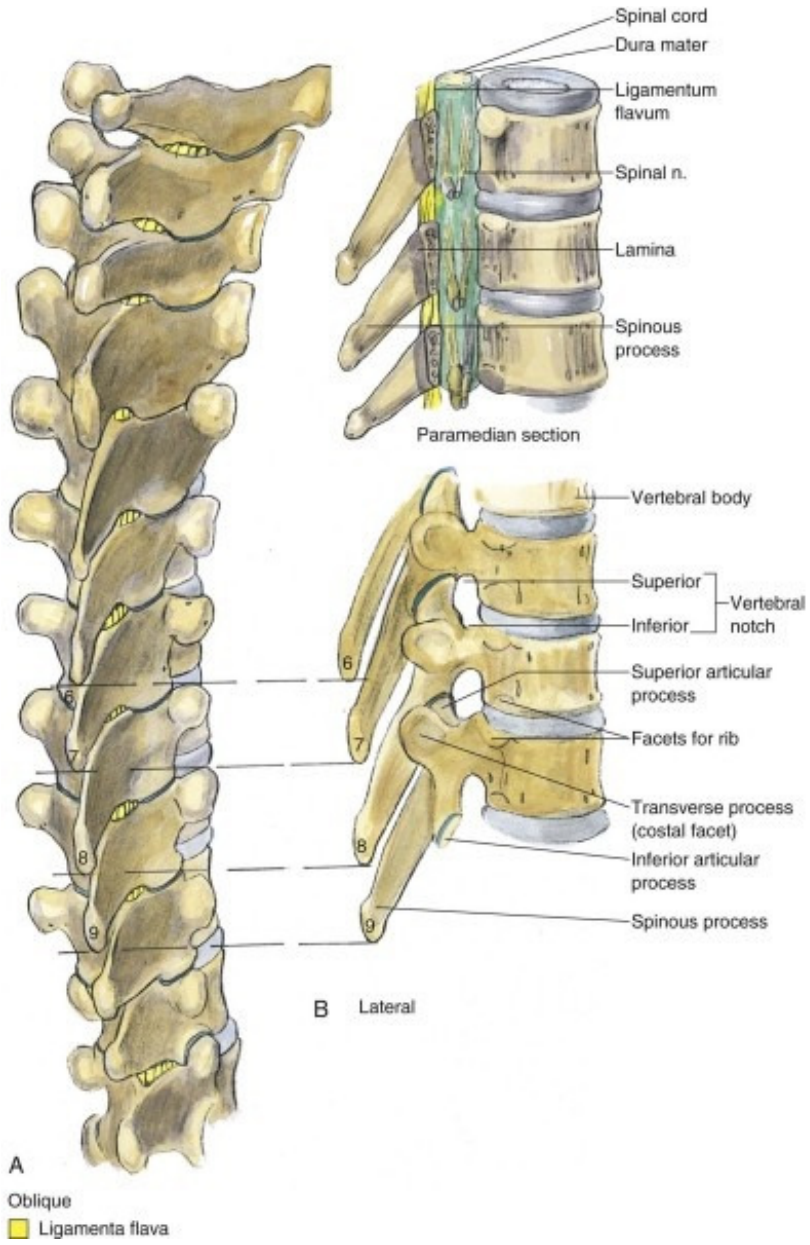
- duramater
- arachnoidmater
- piamater.

The duramater is attached to the margins of foramen magnum above and ends below at the lower border of the second sacral vertebra. The anterior and posterior nerve roots from the spinal cord pierce the investing layer of duramater and carry the prolongation (dural cuff) which blends with the perineurium of the mixed spinal nerve.

The arachnoid mater is a thin transparent sheath closely applied to duramater. The subdural space is a potential space which contains only small amount of serous fluid to allow the dura and arachnoid to move over each other.

The piamater closely invests the cord and sends delicate septa into its substances. From each lateral surface of the piamater, a fibrous band, the denticulate ligament projects into the subarachnoid space. Inferiorly the piamater ends as a prolongation termed as filum terminale which penetrates the distal end of dural sac and is attached to the periostium of coccyx.

The subarachnoid space is filled with the cerebrospinal fluid and it contains the spinal nerve roots and the denticulate ligament. Lumbar puncture is routinely done below the second lumbar vertebra to L5-S1 interspace to avoid damaging the spinal cord which ends at the lower border of first lumbar vertebra.

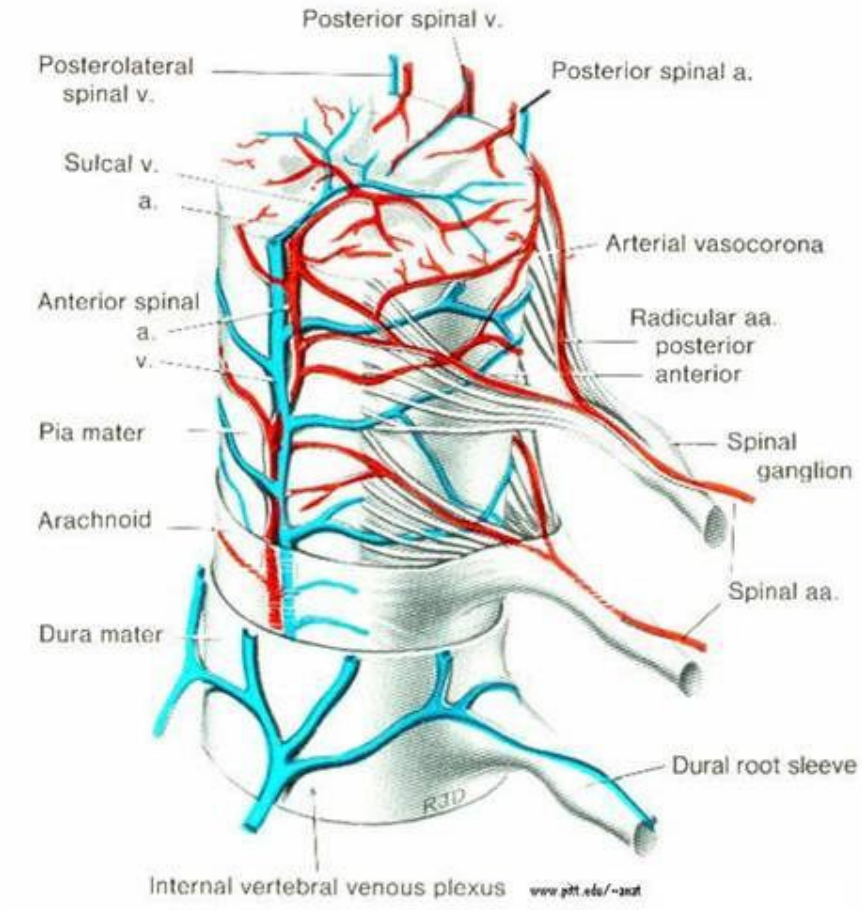


Blood supply of spinal cord[17]

Blood supply of spinal cord is mainly from three longitudinal arterial channels namely

- One anterior spinal artery
- Two posterior spinal arteries

The main source of blood supply to the spinal arteries is from the vertebral arteries. However it reaches only up to the cervical segment of the cord. The spinal arteries also receive blood through radicular arteries that reaches the cord along the roots of spinal nerves. These radicular arteries from the vertebral, ascending cervical, deep cervical, intercostals, lumbar and sacral arteries.



Only few of these radicular arteries are larger in size. The arteria radicularis magna, or artery of Adamkiewicz, the largest of the radicular arteries and it may be responsible for supplying blood to as the lower two-thirds of the spinal cord. Its position is variable.

There is no anastamosis between the anterior spinal artery and the posterior spinal artery. So the occurrence of thrombosis in any of these arteries will cause spinal cord infarction.

Venous drainage of the spinal cord is mainly through six longitudinal venous channels. They are anteromedian and posteromedian venous channels which lie in the midline and two paired anterolateral and posterolateral channels. These channels join together and form a venous plexus, from here the venous blood drains through the radicular vein into segmental veins; the vertebral veins in the neck, the azygos veins in the thorax, lumbar veins in the abdomen and lateral sacral veins in the pelvis.

CEREBROSPINAL FLUID[17]

The cerebrospinal fluid is an ultrafiltrate of plasma secreted by choroid plexus of third, fourth and lateral ventricles at a rate of 0.3 to 0.5ml/min. The average volume ranges from 120 to 150 ml, of which 25 ml is in the cerebral subarachnoid space, 35 ml in the ventricles and about 75 ml is in the spinal subarachnoid space . It is a colourless liquid with slight opalescence due to globulin.

Circulation of cerebrospinal fluid

From the lateral ventricles it enters the 3rd ventricles through the interventricular foramina. Then it flows through the cerebral aqueduct and it reaches the 4th ventricle. Through the foramen of magendie and luschka in the roof of the 4th ventricle it enters the subarachnoid space and circulates over the cerebral hemispheres and around the spinal cord.

Physical Characteristics of Cerebrospinal Fluid

Ph	: 7.4
Specific gravity at body temperature	: 1.007
Specific gravity at 4 degree Celsius	: 1.0003
Density	: 1.0003gm/ml
Baricity	: 1.000
Pressure in supine position	: 8 – 12 mm of hg
Cells	: 3 – 5 / cu.mm
Proteins	: 20mg / dl
Glucose	: 45 – 80 mg/dl

Absorption

The main site of cerebrospinal fluid absorption is into the venous system through the arachnoid villi and arachnoid granulations. These are most numerous in superior saggital sinus and its lateral lacunae. Approximately 300-380 ml of cerebrospinal fluid enters venous circulation each day.

It plays an important role in spinal anaesthesia as a media for dispersion of the local anaesthetic drug to the spinal nerve. Specific gravity of the injected solution is an important factor in determining the spread of the local anaesthetic drug in the subarachnoid space.

SITE OF ACTION OF LOCAL ANAESTHETIC DRUGS[18]

Local anaesthetic solution injected into the subarachnoid space mixes with the cerebrospinal fluid and comes into contact with the spinal cord and the peripheral nerve roots. The nerve roots leaving the spinal canal are readily exposed to the local anaesthetic solution as they are not covered with epithelium.

Zone of Differential Blockade

In subarachnoid block, sympathetic fibres are blocked two to six segments higher than the sensory fibres. Sympathetic block will be greater when more concentrated solutions are used or when adrenaline is added. Motor block will be two segments below the sensory block.

Nerve fibres are blocked in the following order [17]

1. Autonomic preganglionic B fibres
2. Temperature fibres- Cold fibres first followed by warm fibres
3. Pinprick fibres
4. Fibres conveying pain greater than pin prick
5. Touch fibres
6. Deep pressure fibres
7. Somatic motor fibres
8. Fibres conveying vibratory sense and proprioceptive impulses.

During recovery, sensations return in the reverse order, but it has been suggested that sympathetic activity returns before sensation.

SPREAD OF LOCAL ANAESTHETICS IN SUBARACHNOID SPACE

The local anaesthetic solution is diluted by CSF and therefore its original concentration is less than the actual mass of drug injected. Spread is also determined by the baricity of the injected solution. Baricity is a ratio comparing the density of a local anaesthetic solution at a specific temperature to the density of CSF at the same temperature.

A hypobaric solution has a baricity less than 1.0000 or specific gravity less than 1.0069 (the mean value of specific gravity). A hyperbaric solution has a baricity greater than 1.0000 or specific gravity more than 1.0069. Hypobaric and Hyperbaric solutions are prepared from isobaric solutions by the addition of various amounts of sterile distilled water and dextrose respectively.

Isobaric solutions do not move under the influence of gravity in the CSF. Hyperbaric solutions, being heavier than CSF, settle to the most dependent aspect of the subarachnoid space, which is determined by the position of the patient. In supine patient, hyperbaric solutions gravitate to the thoracic kyphosis. Hypobaric solution floats up against the gravity to the nerves innervating the surgical site.

FATE OF LOCAL ANAESTHETICS IN SUBARACHNOID SPACE

After injection of local anaesthetic solution into subarachnoid space, its concentration falls rapidly. The initial steep fall is due to mixing with CSF and subsequent absorption into nerve roots and spinal cord. The removal of local anaesthetic solution following subarachnoid injection is primarily by vascular absorption.

Depending on the type of the drug used, it is metabolized in plasma by pseudo cholinesterase or in the liver. The addition of a vasoconstrictor to the local anaesthetic solution will decrease the absorption of the drug and thus increase the duration of anaesthesia.

PHYSIOLOGICAL EFFECTS OF SUBARACHNOID BLOCK

Cardiovascular effects

Vasomotor tone is determined by sympathetic fibers arising from T5 to L1 and innervating arterial and venous smooth muscle. Hence sympathetic block will cause a decrease in blood pressure that may be accompanied by a decrease in heart rate. With high sympathetic block, sympathetic cardiac accelerator fibers arising at T1-T4 are blocked, leading to decreased cardiac contractility. Bezold-Jarisch reflex has been implicated as a cause of bradycardia, hypotension and cardiovascular collapse after central neuraxial anaesthesia, in particular spinal anaesthesia.

Respiratory effects

Even with high thoracic levels, the tidal volume remains unchanged. A small decrease in vital capacity is due to paralysis of abdominal muscles necessary for forced exhalation and not due to phrenic nerve involvement or impaired diaphragmatic function. Effective coughing and clearing of secretions may get affected with higher levels of block. Respiratory arrest associated with spinal anaesthesia is rare and is due to hypo perfusion of respiratory centers in brain stem.

Gastrointestinal function

Nausea and vomiting is seen in upto 20% of patients. It is due to gastrointestinal hyperperistalsis caused by unopposed parasympathetic activity. Vagal tone dominance results in a small contracted gut with active peristalsis and can provide excellent operative conditions. Hepatic blood flow will decrease with reductions in mean arterial pressure.

Renal function

Renal function has a wide physiological reserve. Decrease in renal blood flow is of little physiological importance. Neuraxial blocks are a frequent cause of urinary retention which delays discharge of outpatients and necessitates bladder catheterization of inpatients.

INDICATIONS FOR SUBARACHNOID BLOCK

Spinal anaesthesia can be administered for surgeries below umbilicus such as

- Lower abdominal surgeries
- Lower limb surgeries
- Urological procedures
- Obstetric procedures
- Gynaecological surgeries
- Perineal and rectal surgeries

CONTRAINDICATIONS FOR SUBARACHNOID BLOCK

The absolute contraindication for subarachnoid block are

- Patient refusal
- Local sepsis

The relative contraindications include

- Raised intracranial pressure
- Coagulopathy
- Neurological disease
- Fixed cardiac output states
- Documented allergy to local anaesthetics
- Major spine deformities or previous surgery on the spine
- Hemodynamic instability

FACTORS INFLUENCING HEIGHT OF ANALGESIA IN SUBARACHNOID BLOCK

- Dose of the drug injected
- Volume of fluid injected
- Specific gravity of the solution

- Position of the patient during injection
- Posture of patient after injection
- Choice of interspace
- Patient factors- Age, Height and Pregnancy

FACTORS NOT INFLUENCING HEIGHT OF ANALGESIA IN SUBARACHNOID BLOCK

- Patient factors- Weight, Sex.
- Barbotage.
- Rate of injection.
- Composition and circulation of cerebrospinal fluid.
- Direction of bevel of the standard needle (although not of the Whitacare needle).

COMPLICATIONS OF SUBARACHNOID BLOCK

The Immediate complications include

- Hypotension
- Bradycardia
- Toxicity due to intravascular injection
- Allergic reaction to local Anaesthetic
- Hypoventilation (brain stem hypoxia)

The late complications include

- Postdural puncture headache
- Retention of urine
- Backache
- Meningitis
- Transient neurological symptoms
- Cauda equine syndrome
- Anterior spinal artery syndrome
- Horner's syndrome

LOCAL ANAESTHETIC DRUGS

Local anaesthetic agents are divided into two groups namely the amides and esters

Esters

- Benzocaine
- Chloroprocaine
- Cocaine
- Cyclomethycaine
- Dimethocaine
- Piperocaine
- Propoxycaine
- Procaine
- Proparacaine
- Tetracaine/Amethocaine

Amides

- Articaine
- Bupivacaine
- Dibucaine

- Etidocaine
- Levobupivacaine
- Lignocaine
- Mepivacaine
- Prilocaine
- Ropivacaine
- Trimecain

Adjuvants used in spinal anaesthesia

Opioids

- Morphine
- Fentanyl
- Sufentanyl
- Diamorphine

Clonidine

Ketamine

Neostigmine

Adrenaline

Phenylepherine

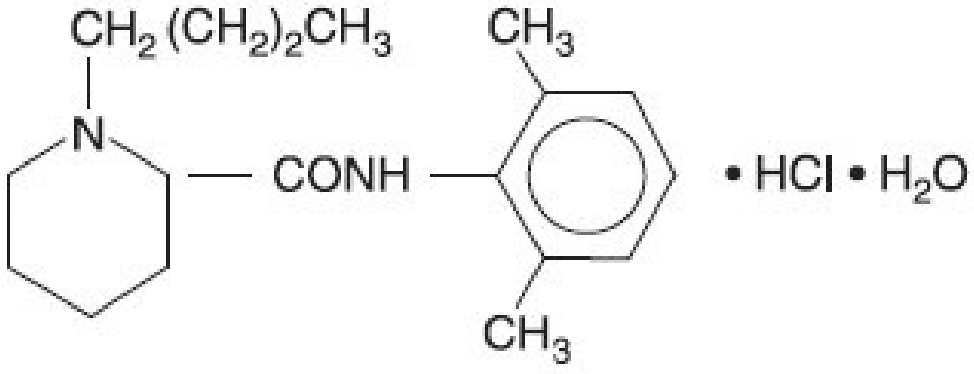
Sodium bicarbonate

PHARMACOLOGY OF BUPIVACAINE[19 20 21]

Bupivacaine, an amino amide local anaesthetic was first synthesized in Sweden by A.F Ekenstam and his colleagues in 1957. First report of its use was in 1963 by L.J Teluvio. It is one of the long acting local anaesthetic agents available, which is extensively used for intrathecal, extradural and peripheral nerve blocks. It is a white crystalline powder soluble in water

CHEMICAL STRUCTURE OF BUPIVACAINE

Bupivacaine has an IUPAC nomenclature of 1-butyl-n-(2,6-dimethylphenyl) piperidine-2-carboxamide.



Physiochemical properties[22]

Molecular formula	: $C_{18}H_{28}N_{2O}HCl$
Molecular weight	: 288.43 g/mol
Protein binding	: 95%
pH of saturated solution	: 5.2
pKa	: 8.1
Specific gravity	: 1.021 at 37 °C

Mechanism of action[23, 24]

Mechanism of action of bupivacaine is similar to that of any other local anaesthetic. The primary action of local anaesthetics is on the cell membrane axon, on which it produces electrical stabilization. Bupivacaine prevents transmission of nerve impulses (conduction blockade) by inhibiting passage of sodium ions through ion-selective sodium channels in nerve membranes.

The sodium channel is a specific receptor for local anaesthetic molecules. Failure of sodium ion channel permeability to increase slows the rate of depolarization such that threshold potential is not reached and thus an action potential is not propagated. Local anaesthetics do not alter the resting transmembrane potential or threshold potential.

The mechanism by which local anaesthetics block sodium conductance is as follows

1. Local anaesthetics in the cationic form act on the receptors within the sodium channels on cell membrane and block it. The local anaesthetics can reach the sodium channel either via the lipophilic pathway directly across the lipid membrane, or via the axoplasmic opening. This mechanism accounts for 90% of the nerve blocking effects of amide local anaesthetics.

2. The second mechanism of action is by membrane expansion. This is a nonspecific drug receptor interaction.

Other site of action targets

- Voltage dependent potassium ion channels
- Calcium ion currents (L-type most sensitive)
- G protein coupled receptors

Dosage depends on

Area to be anaesthetized

Number of nerve segments to be blocked

Individual tolerance

Technique of local anaesthesia

Vascularity of area

AVAILABILITY

Ampoules – 0.5% Bupivacaine hydrochloride 4cc

_ 0.5% Bupivacaine with dextrose (heavy) 4cc

Vials _ 0.25% and 0.5% Bupivacaine hydrochloride 30 cc

Dosage _ Maximum dosage 3mg/kg body weight.

ANAESTHETIC POTENCY

Hydrophobicity appears to be a primary determinant of intrinsic anesthetic potency and Bupivacaine is highly hydrophobic, hence is very potent.

ONSET OF ACTION

The onset of conduction blockade is dependent on the dose or concentration of the local anaesthetic. The onset of action of Bupivacaine is between 4 – 6 minutes and maximum anaesthesia is obtained between 15 – 20 minutes.

DURATION OF BLOCK

The duration of anaesthesia varies according to the type of block. The average duration of peridural block is about 3.5 – 5 hours, for nerve block 5 – 6 hours and for intrathecal block, it is about 1.5 to 2 hours.

PHARMACOKINETICS

The concentration of Bupivacaine in blood is determined by the amount injected, the rate of absorption from the site of injection, the rate of tissue distribution and the rate of biotransformation and excretion of Bupivacaine.

Bupivacaine can be detected in the blood within 5 minutes of infiltration or following epidural or intercostal nerve blocks. Plasma levels are related to

the total dose administered. Peak levels of 0.14 to 1.18 µg/ml were found within 5 mins to 2 hrs, and they gradually declined to 0.1 to 0.34 µg/ml by 4 hrs.

Plasma binding

In plasma, drug binds avidly with protein to the extent of 70 -90%. The rank order of protein binding for this and its homologues is bupivacaine, mepivacaine, lidocaine. Conversely, the unbound active fraction is one seventh of lidocaine and one fifth of mepivacaine.

Absorption

The site of injection, dose and addition of a vasoconstrictor determine the systemic absorption of Bupivacaine .The maximum blood level of Bupivacaine is related to the total dose of drug administered from any particular site. Absorption is faster in areas of high Vascularity.

Toxicity

The toxic plasma concentration is set at 4 - 5 µg/ml. Maximum plasma concentration rarely approach toxic levels.

Distribution

Rapid distribution phase: (α)

In this phase the drug is distributed to highly vascular region.

Half life of α- being 2.7 minutes.

Slow disappearance phase: (β)

In this phase the drug distributes to slowly equilibrating tissues.

Half life of (β)- being 28 minutes.

Biotransformation and excretion phase: (δ)

Half life of δ is 3.5 hours, clearance is 0.47litre/minute.

More highly perfused organs show higher concentrations of the drug. Bupivacaine is rapidly excreted by lung tissue. Though skeletal muscle does not show any particular affinity for bupivacaine it is the largest reservoir of the drug.

Biotransformation and Excretion

Bupivacaine undergoes enzymatic degradation primarily in the liver. The excretion occurs primarily via the kidney. Renal perfusion and factors affecting urinary pH affect urinary excretion. Less than 5% of Bupivacaine is excreted via the kidney unchanged through urine.

The major portion of injected agent appears in urine in the form of 2,6 pipecolyoxylidine (ppx) which is a n-dealkylated metabolite of bupivacaine. Renal clearance of the drug is related inversely to its protein binding capacity and pH of urine.

PHARMACODYNAMICS

Central Nervous System

Bupivacaine readily crosses the blood brain barrier causing CNS depression following higher doses. The initial symptoms involve feeling of light-headedness and dizziness followed by visual and auditory disturbances. Disorientation and drowsiness may occur. Objective signs are usually

excitatory in nature, which includes shivering, muscular twitches and tremors, initially involving muscles of the face (perioral numbness) and part of extremities.

At still higher doses cardiovascular or respiratory arrest may occur. Acidosis increases the risk of CNS toxicity from Bupivacaine, since an elevation of PaCO2 enhances cerebral blood flow, so that more anaesthetic is delivered rapidly to the brain

Autonomic nervous system

Bupivacaine does not inhibit the Noradrenaline uptake and hence has no sympathetic potentiating effect. Myelinated preganglionic B fibers have a faster conduction time and are more sensitive to action of Bupivacaine. When used for conduction blockade, all local anaesthetics, particularly Bupivacaine produces higher incidence of sensory than motor fibers.

Cardiovascular System

The primary cardiac electrophysiological effect of a local anaesthetic is a decrease in the maximum rate of depolarization in Purkinje fibers and

ventricular muscle. This action by Bupivacaine is far greater compared to Lignocaine. Also, the rate of recovery of block is slower with Bupivacaine.

Therefore there is complete restoration of Vmax between action potential particularly at higher rates. Therefore Bupivacaine is highly arrythmogenic. Bupivacaine reduces the cardiac contractility by blocking the calcium transport. Low concentration of Bupivacaine produces vasoconstriction whereas high doses cause vasodilatation.

Respiratory System

Respiratory depression may be caused if excessive plasma level is reached which in turn results in depression of medullary receptor center. Respiratory depression may be also caused by paralysis of respiratory muscles of diaphragm as may occur in high spinal or total spinal anaesthesia.

Adverse Effects

Adverse effects are encountered in clinical practice mostly due to overdose, inadvertent intravascular injection or slow metabolic degradation.

Central nervous system

It is characterized by excitation or depression. The first manifestation may be nervousness, dizziness, blurring of vision or tremors, followed by drowsiness, convulsions, unconsciousness and respiratory arrest.

Cardiovascular system

Myocardial depression, hypotension, arrhythmia, ventricular type conduction defect, SA node depression and cardiac arrest

Allergic reactions

Urticaria

Bronchospasm

Hypotension

Others - nausea, vomiting, chills, constriction of pupil and tinnitus.

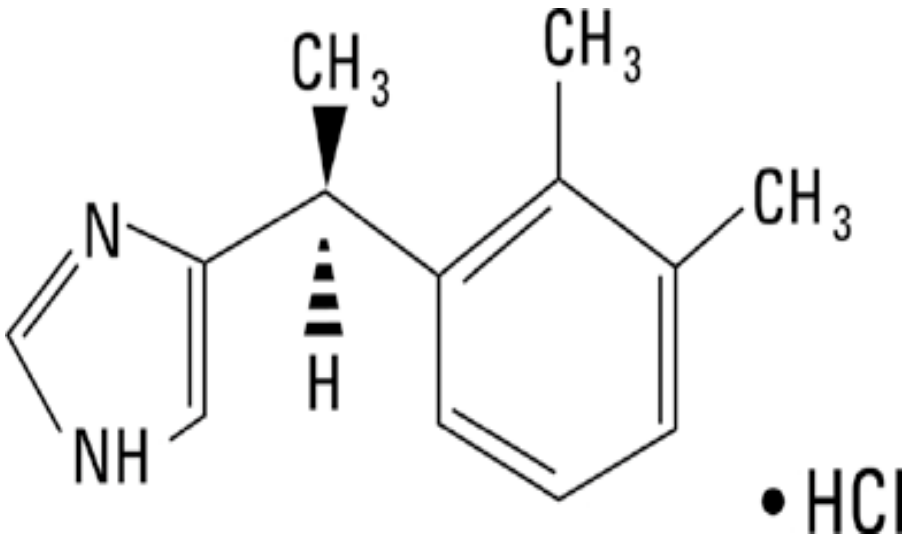
TREATMENT OF ADVERSE EFFECTS

Treatment is mainly symptomatic. One should be prepared to maintain circulation and to support ventilation with oxygen or controlled ventilation, if required. Supportive treatment with IV fluids and vasopressors restore the cardiovascular stability. Convulsions may be controlled with Diazepam (0.1- 0.2mg/kg) or Thiopentone (2-3 mg/kg) or a muscle relaxant and controlled ventilation with oxygen.

Corticosteroids, if allergic reactions are suspected. Treatment of ventricular fibrillation and tachycardia by Amiodarone (5mg/kg iv) or defibrillation (2-6 joule/kg).

PHARMACOLOGY OF DEXMEDETOMIDINE[25 26]

Dexmedetomidine is the d-enantiomer of medetomidine, belongs to the imidazole subclass of α_2 receptor agonists. It is a more selective α_2 agonist with a 1600 greater selectivity for the α_2 receptor compared with the α_1 receptor. It was introduced in clinical practice in 1999 and the only FDA approved use of dexmedetomidine is for sedation in mechanically ventilated patients in intensive care unit. It is now being used off-label outside of the ICU in various settings, including sedation and adjunct analgesia in the operating room, sedation in diagnostic and procedure units, and for other applications.



MECHANISM OF ACTION

Alpha$_2$ adrenoreceptors are membrane-spanning G proteins. There are three subtypes of α_2 adrenergic receptors in humans: α_{2A}, α_{2B}, and $\alpha_{2C.}$ The α_{2A} receptors are distributed mainly in the periphery, likewise α_{2B} and α_{2C} receptors are primarily distributed in spinal cord and brain.

Postsynaptic α_2 receptors in the peripheral blood vessels produce vasoconstriction, whereas α_2 receptors located in the presynaptic region inhibit the release of norepinephrine, potentially attenuating the vasoconstriction. These receptors are involved in the sympatholysis, sedation, and antinociceptive effects of α_2 receptors.

PHARMACOKINETICS

Dexmedetomidine when injected intravenously, it is rapidly distributed in the body and it is metabolized mainly in the liver and excreted in urine and faeces. Dexmedetomidine is 94% protein bound. The elimination half-life of dexmedetomidine is around 2 hours and with a context-sensitive half-time of 4 minutes to 250 minutes after an 8-hour infusion. Volume of distribution is 118 litres. Clearance is estimated to be approximately 39litres/ hour.

Effects on the central nervous system

Sedation

Dexmedetomidine acts on the alpha 2 receptors in locus ceruleus and causes sedation as well as hypnosis. It exerts sedative effect by acting through the endogenous sleep-promoting pathways.

Analgesia

Analgesia produced by dexmedetomidine is complex and not clearly known. The spinal cord is thought to be the primary site of action. It causes analgesia when injected either in intrathecal or epidural space.

Respiratory System

When dexmedetomidine is given at doses required to produce significant sedation it reduces minute ventilation, but the response to increase in carbon dioxide concentration is preserved. Ventilatory changes caused by dexmedetomidine is identical to the changes that appear during normal sleep.

Effects on the Cardiovascular System

Dexmedetomidine causes a decrease in heart rate, myocardial contractility, cardiac output, systemic vascular resistance and blood pressure myocardial contractility and cardiac output. Dexmedetomidine when given in bolus dose has shown a biphasic response. Rapid injection of dexmedetomidine in a dose of 2 µg/kg causes a brief rise in the blood pressure (22%) and a decrease in the heart rate (27%) from the base line valve.

This brief rise in blood pressure is due to the stimulation of peripheral alpha 2 receptors which causes vasoconstriction. After 15 minutes the heart rate came back to the baseline level, and blood pressure gradually declined to approximately 15% below baseline by 1 hour.

USES

Dexmedetomidine is used for sedation in mechanically ventilated patients and for procedural sedation prior to or during surgery.

In operating room, it is used for premedication and a sole anaesthetic in monitored anaesthesia care. It is also used as an adjunct with local

anaesthetic drugs in peripheral nerve block, intravenous regional anaesthesia, epidural and spinal anaesthesia.

Intensive care unit

Dexmedetomidine has several advantages over propofol while sedating postoperative patients in intensive care units. It reduces opioids consumption, PaO_2/FIO_2 ratio was significantly higher and heart rate was slower in dexmedetomidine group. Due to its unique character of providing good sedation with less respiratory depression it can be used while weaning patients from the ventilator.

Anaesthesia

Dexmedetomidine when used as a premedicant it reduces the requirements of induction agents, volatile anaesthetics and opioids. It suppresses the hemodynamic response to intubation. When used in ophthalmic cases it reduces the intraocular pressure and catecholamine secretion is reduced. Perioperative analgesic requirements are less, and recovery is more rapid. In a morbidly obese patient, the narcotic-sparing

effect of dexmedetomidine was evident in the intraoperative and postoperative period after bariatric surgery.

Dexmedetomidine has been successfully used in the treatment of withdrawal of narcotics, benzodiazepines, alcohol, and recreational drugs. It is also used for procedural sedation in paediatric patients.

Dosage and administration:

For adults, dexmedetomidine is administered intravenously at a loading dose of 0.5 to 1 µg/kg as a slow infusion over a period of ten minutes, followed by a maintenance infusion of 0.2 to 0.7 µg/kg/hr.

Dexmedetomidine should be diluted in 0.9 % normal saline for infusion. Dexmedetomidine is recommended for infusion lasting up to 24 hrs. It is freely soluble in water.

Adverse effects:

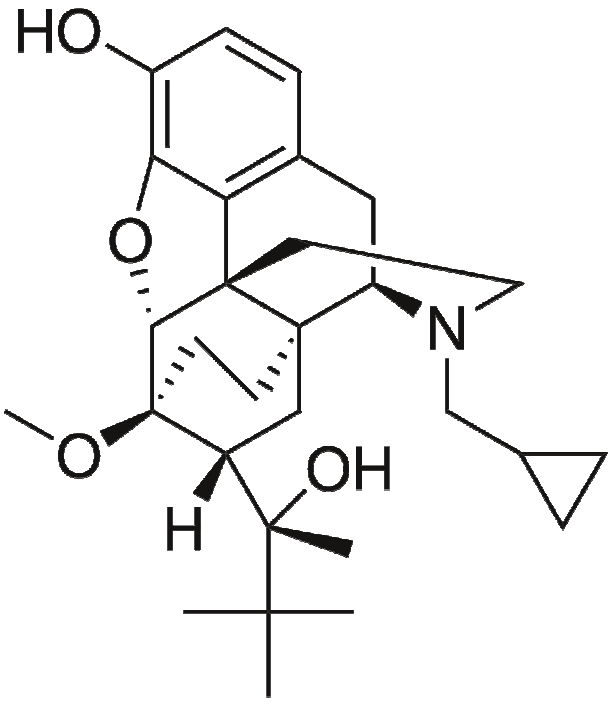
Major adverse effects include transient hypertension, hypotension haemorrhage, bradycardia, atrial fibrillation, sinus tachycardia, sinus arrest, ventricular tachycardia, myocardial infarction, agitation, confusion, delirium, hallucination, illusion and dry mouth.

PHARMACOLOGY OF BUPRENORPHINE[18]

Buprenorphine (CN-L-cyclopropyl methyl oripavin) is a potent semisynthetic highly lipophytic ring C bridge oripavine derivative of thebaine with narcotic agonist and antagonist activity. It is 25 to 40 times more potent than Morphine in analgesic effect.

Chemical structure

Buprenorphine HCL is 17 cyclopropyl methyl α1,1-dimethyl ethyl 4,5-epoxy-18,19-dihydro 3-hydroxy 6 methoxy -2-methyl-6,14 ethanomorphinan-7 methanol hydrochloride.



PHARMACOLOGICAL ACTIONS

(1) Central nervous system

Buprenorphine produces typical dose related morphine like subjective effects. They are slower in onset but longer duration. Early receptor binding studies suggested that Buprenorphine was a selective mu receptor agonist. In rodents, the dose response curves for Buprenorphine induced analgesia and catalepsy is bell shaped. It has a high affinity for the mu, delta and kappa receptors.

In receptor binding studies Buprenorphine behaves like an antagonist – Judged by the effect of Na++ ion affinity. Due to its no receptor agonist action it may cause symptoms of abstinence in patients who have been receiving Morphine like drugs. Buprenorphine is effective in relieving pain moderate to severe degree associated with surgical procedures, (Abdominal, thoracic, orthopaedic and hysterectomy) cancer pain neuralgias, renal colic, labour pain and myocardial infarction.

It is more potent than morphine, pethidine, and pentazocine and the duration of analgesia is longer than all. Buprenorphine is relatively free from

dysphoria and psychotomimetic actions. Hallucinations was produced in only 0.9% of individuals.

(2) Respiratory system

The subjective respiratory depressant effects are unequivocally slower in onset and lasts longer than those of morphine. Maximum respiratory depression is observed at about 3 hours. Respiratory depression has not been observed in clinical trial.

Significant respiratory depression appears to be dose related. In anaesthetized patients Buprenorphine decreases both respiratory rate and volume. In postoperative period, Buprenorphine produces tendency towards respiratory acidosis and small decreases in respiratory rate (15%) and minute volume (16%).

(3) Cardiovascular system

In equivalent doses all the cardiovascular effects are similar to those of Morphine. There is significant reduction in heart rate (16%) with only minor decrease in systolic & diastolic pressure. In surgical or myocardial infarct patients, there is dose related decrease in systolic and diastolic pressure (10 to

25%), oxygen consumption (40%), left ventricular work (19%) and heart rate (24%) as well as compensatory increase in stroke volume. There is small decrease in pulmonary artery blood pressure. Myocardial contractility is not affected. It appears to be a safe analgesic for patients with a recent myocardial infarction.

(4) Alimentary system

It does not necessarily produce constipation. It causes nausea, vomiting in 10 to 20% of individuals. It increases intrabiliary pressure.

REVERSIBILITY OF BUPRENORPHINE EFFECT

By narcotic antagonist.

Naloxone only partially reverses the respiratory depression produced by Buprenorphine, although this effect was temporarily reversible with a respiratory stimulant drug, Doxapram. Such treatment was apparently not completely satisfactory.

TOLERANCE, PHYSICAL DEPENDENCE AND LIABILITY FOR ABUSE

In post addicts patients, subcutaneous dose of Buprenorphine doses (ranging from 0.2 mg to 2 mg) produce typical morphine like effects. Buprenorphine was given subcutaneously for 40 to 50 days in a daily dose of 8 mg. Subjects and observer identified Buprenorphine as a Morphine like agent.

Subsequent administration of Naloxone did not produce abstinence syndrome. Buprenorphine resulted in very slowly emerging signs of withdrawal indicating a very long duration of action with very slow dissociation from opiate receptor sites. Overall potential for above of Buprenorphine is less than that of morphine.

PHARMACOKINETICS

Absorption

It is rapidly absorbed after intramuscular injection. Peak plasma levels are equal to those achieved with intravenous injection. Absorption is variable in sublingual dose. Average peak level is 3 hours and absorption completes within 5 hours. However, analgesia is attained within 15 minutes to 20 minutes and effect last longer than plasma levels. Thus appears to be no direct

relationship between plasma levels and pharmacological actions. Bioavailability after sublingual dose in 50% occur with other strong analgesics such as Morphine, Pethidine, and Pentazocine.

Precautions

It may infrequently affect respiration and hence should be used with care in treating patients with impaired respiratory function. Ambulant patients should be warned not to drive car as it can cause drowsiness. As it has antagonist properties, it may precipitate withdrawal syndrome in narcotic addicts.

The intensity and duration of action may be affected in patients with impaired liver functions. It should be used with caution in patients receiving MAO Inhibitors. It is relatively contraindicated in patients with head injuries. There is no absolute contraindications. It is not at present recommended in children and pregnant patients.

Routes of administration– Sublingual, Parenteral, Intramuscular, Intravenous, Subcutaneous, through Brachial plexus block, Intrathecally, Epidurally.

USES

Post operative pain.

Premedication before surgery.

Component of balance anaesthesia.

To reverse anaesthetic effects of fentanyl.

REVIEW OF LITERATURE

Mahima Gupta et al [27] ***in 2013*** conducted a double blinded study to evaluate and compare the characteristics of subarachnoid blockade, hemodynamic stability and adverse effects of intrathecal buprenorphine and intrathecal dexmedetomidine as an adjuvant to 0.5% hyperbaric bupivacaine for lower abdominal surgeries.

Sixty patients were divided into two groups: Group B and Group D of thirty each. Group B received sixty µg of buprenorphine with 3 cc (15 mg) of 0.5% heavy bupivacaine. Group D received 5 µg of Dexmedetomidine with 3cc(15 mg) of 0.5% heavy bupivacaine.

The onset of sensory and motor blockade in both Dexmedetomidine and buprenorphine were comparable. The duration of motor and sensory block in dexmedetomidine group was 413 minutes and 451 minutes which was significantly different from 205 minutes and 226 minutes of buprenorphine group. Similarly duration of analgesia was 493 minutes in dexmedetomidine group as compared to 289 minutes of buprenorphine group.

They concluded that intrathecal dexmedetomidine 5 µg when compared to intrathecal buprenorphine sixty µg causes prolonged duration of sensory and motor block.

The requirement of additional sedation and rescue analgesia is less in dexmedetomidine group and the haemodynamics are similar in both the groups without causing any significant side effects.

Sapkal pravin S et al [34] **in 2013** conducted a study to evaluate and compare the efficacy, duration of post operative analgesia and adverse effects of intrathecal clonidine 60 µg and intrathecal Buprenorphine 60µg used as adjuvants in spinal anaesthesia for lower limb orthopaedic surgeries.

Total 80 male patients aged 20 to 60 years belonging to ASA grade I and II undergoing elective or emergency lower limb orthopaedic surgeries were randomly allocated into two groups. Group C received 3ml 0.5% bupivacaine with 60 µg clonidine, Group B received 3ml 0.5% bupivacaine with 60 µg buprenorphine. Duration of subarachnoid block , total analgesia, effective analgesia, number of rescue analgesics and adverse effects were assessed and compared in both groups.

In group B , the duration of subarachnoid block is 161.3 ±13.9 minutes whereas in group C , the duration of subarachnoid block was 289.6±12.9 minutes .In group B , the duration of effective analgesia was 818.9±135.5 minutes whereas in group C , the duration of effective analgesia was 686.5±41.9 minutes. In group B , the duration of total analgesia was 488.2±72.3 minutes whereas in Group C , the duration of total analgesia was

468.1±46.1 minutes. In group B , the nausea was noted in 17.5% of patients, whereas in group C , it was noted in 7.5% of patients. Vomiting was present in 5% of patients in group B whereas none of the patients vomited in clonidine group. Somnolence was noticed slightly higher in buprenorphine group i.e., 7.5% while 2.5% in clonidine group.

This study concludes that intrathecal clonidine 60 µg significantly prolongs duration of spinal anaesthesia and quality of analgesia was acceptable to patients in both groups though VAS assessment was better in buprenorphine group.

Alka shah et al [33] in 2012 conducted a study on 50 ASA 1 and 2 patients planned for lower limb and lower abdomen surgery. The aim of this study was to evaluate the hemodynamic effects intra operatively and the duration of postoperative analgesia.

Each patient received 0.75% isobaric ropivacaine 4ml plus 5µg dexmedetomidine at the intervals of 1 minute, 2 minute, 5 minute, 10 minute, 20 minute, 30 minute, and 1 hour, 2 hour and 3 hour reading of pulse rate and blood pressure were recorded. Postoperatively pain scores were recorded by using visual analogue scale. There were no significant changes in systolic and diastolic blood pressure after induction. This combination provides better

postoperative analgesia and reduced requirement of diclofenac injection in first 24 hours.

They concluded that 5µg dexmedetomidine seems to be an attractive alternative as an adjuvant to spinal ropivacaine in surgical procedures, especially those requiring long time. This combination (ropivacaine and dexmedetomidine) provides very good quality of hemodynamic stability. It has excellent quality of post operative analgesia with minimal side effects.

Rajni Gupta et al [9] in 2011 Conducted a comparative study of intrathecal Dexmedetomidine and Fentanyl as adjuvants to Bupivacaine to evaluate the onset, duration of sensory and motor block, hemodynamic effect, post-operative analgesia and adverse effects.

Sixty patients scheduled for lower abdominal surgeries were randomly allocated into 2 groups of 30 each. Group D recieved 12.5mg hyperbaric Bupivacaine with 5µg Dexmedetomidine. Group F received 12.5mg hyperbaric bupivacaine with 25 µg Fentanyl intrathecally.

The mean time of sensory regression to S1 was 476 ± 23min in Dexmedetomidine and 187 ± 12 min in Fentanyl group. Regression to motor block was 421 ± 21min in Dexmedetomidine and 149 ± 18min in Fentanyl group.

They inferred that intrathecal Dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand for rescue analgesics in 24 hours as compared to fentanyl.

Hala E A Eid [29] et al in 2011 conducted a prospective randomised double blinded study to evaluate the effect of intrathecal administration of dexmedetomidine on the duration of sensory and motor block and postoperative analgesic requirements produced by spinal bupivacaine.

Forty eight patients schedule for anterior cruciate ligament reconstruction were randomized to one of the three groups receiving 10µg Dexmedetomidine in first group, 15µg Dexmedetomidine in second group and normal saline in the third group with 3ml of 0.5% hyperbaric bupivacaine. Dexmedetomidine significantly prolonged time to 2 segment regressions, sensory regression to S1 regression of motor block to modified Bromage 0, time to first rescue analgesia and decreased post-operative pain scores.

They concluded that intrathecal Dexmedetomidine in doses of 10µg and 15µg significantly prolong the anaesthetic and analgesic effects of spinal hyperbaric Bupivacaine in a dose dependant manner.

Shukla et al [32] **in 2011** conducted a prospective randomised double blind study to evaluate the onset and duration of sensory and motor block, peri-

operative analgesia and adverse effects of Dexmedetomidine and magnesium sulphate given intrathecally with 0.5% hyperbaric Bupivacaine for spinal anaesthesia.

90 patients of ASA Grade 1 and 2 scheduled for lower abdominal and lower limb procedures were prospectively studied. Patients were randomly allocated into 3 Groups of 30 each. Group D received 3 ml hyperbaric Bupivacaine + 0.1 ml (10 μg) Dexmedetomidine. Group M received 3 ml of hyperbaric Bupivacaine + 0.1 ml (50 mg) magnesium sulphate. Group C received 3 ml of hyperbaric Bupivacaine + 0.1 ml normal saline.

The onset time to reach peak sensory and motor level, regression time for sensory and motor block, haemodynamic changes and side effects were recorded. The onset time of sensory block to reach T_{10} dermatome was 2.27 ± 1.09 minutes in group D, 6.46 ± 1.33 in Group M and 4.14 ± 1.06 minutes in Group C. The onset time to reach Bromage 3 was 3.96 ± 0.92 minutes in Group D, 7.18 ± 1.38 minutes in Group M and 4.81 ± 1.03 in Group C. The regression time of sensory block was 352 ± 45 minutes in Group D, 265 ± 65 in Group M and 194 ± 55 minutes in Group C. The regression time of motor block for Group D was 331 ± 35, 251 ± 51 for Group M and 140 ± 34 for Group C.

There was no significant differences in the mean values and MAP the first hour after performing spinal anaesthesia and first hour in the PACU between 3 groups. The SPO_2 was more than 95% in all patients in the 3 groups

either in the intraoperative or in the PACU time. 24 hours and 2 weeks following discharge, follow up did not show any neurological impairment related to spinal anaesthesia, back, buttock or leg pain, head ache or any neurological symptom.

They concluded that intrathecal DXM supplementation of spinal block seems to be a good alternative to intrathecal Mg as it produces earlier onset and prolonged duration of sensory and motor block without associated significant haemodynamic alterations.

Sheikh kiran et al [8] **in 2010** conducted a prospective randomised double blind study to assess the efficacy 0f intrathecal buprenorphine for postoperative pain relief and to study the incidence of side effects.

100 patients of ASA 1 and 2 between the age group of 18- 60 years, who underwent surgery of the lower extremities and lower abdomen were randomly allocated into 2 groups of 50 each. Group A received 15 mg heavy bupivacaine plus 0.2 ml normal saline. Group B received 15 mg of heavy bupivacaine plus 1µg /kg of buprenorphine 0.2ml intrathecally upto a maximum of 50µg.

The average time of onset of sensory block was 3.78 ± 0.97 min in Group A and 3.66 ± 1.008 in Group B. The mean duration of analgesia was

195.2 ± 29.52 in Group A and 475.6 ± 93.7 in Group B. The mean pulse rate at 0 min was 81.3 ± 7.91 in Group A and 79.16 ± 6.156 in Group B and the difference in pulse rate at 0,5, 10, 30 and 60 minutes respectively between both groups were not statistically significant. There were 5 cases of hypotension and 1 case of nausea vomiting in Group A Whereas in Group B, there were 6 cases of hypotension, 2 cases of vomiting and 2 cases of shivering.

They concluded that intrathecal Buprenorphine is an effective analgesic suitable for the management of postoperative pain.

Subhi M Al-Ghanem et al [31] **in 2009** conducted a prospective randomised double blinded study to compare the effect of adding Dexmedetomidine versus fentanyl to intrathecal 0.5% isobaric Bupivacaine on spinal characteristics in gynaecological procedures.

Seventy eight patients (ASA 1 to 3) were prospectively studied. Group D received isobaric bupivacaine 10 mg and Dexmedetomidine 5µg (2.5ml) and Group F received isobaric bupivacaine 10 mg and fentanyl 25 microgram (2.5ml) .

The onset time of sensory block to reach T10 was 7.5 ± 7.4 minutes for Group D and 7.4 ± 3.3 minutes for Group F. The time to reach maximum sensory block was 19.34 ± 2.87 minutes for Group D and 18.39 ± 2.46 minutes for Group F. The onset time of motor block was 14.4 ±6.7 minutes in Group

D and 14.3± 5.7 minutes in Group F. The duration of motor block was 240 ± 64 minutes in Group D and 155 ± 46 minutes in Group F. The sensory regression to S1 segment was 274.8 ± 73.4 minutes in Group D and 179.5 ±47.4 minutes in Group F .The peak sensory level was T6 in both the groups.

They concluded that 5 µg of dexmedetomidine seems to be an attractive alternative as adjuvant to spinal bupivacaine in surgical procedures especially in those that need quiet long time with minimal side effects and excellent quality of spinal analgesia.

Mahmoud M Al-Mustafa et al [30] **in 2008** conducted a study to determine the effect of adding different doses of dexmedetomidine to isobaric bupivacaine for patients undergoing urological procedures under spinal anaesthesia .

Sixty six patients were randomly assigned into 3 groups. Group N received Bupivacaine 12.5mg with saline. Group D5 received 12.5mg Bupivacaine with 5µg Dexmedetomidine. Group D10 received 12.5mg Bupivacaine with 10µg Dexmedetomidine. The mean time of sensory block to reach T10 dermatome was 4.7 ±2 minutes in D10 group, 6.3 ±2.7 minutes in D5 group and 9.5 ± 3 minutes in Group N .

The mean time to reach Bromage 3 scale was 10.4 ± 3.4 minutes in group D10, 13.0 ± 3.4 minutes in Group D5 and 18.0 ± 3.3 minutes in Group

N. The regression time to reach S1 dermatome was 338.9 ± 44.8 minutes in Group D10, 277.1±23.2 minutes in D5 and 165.5 ± 32.9 minutes in Group N . The regression to Bromage 0 was 302.9± 36.7 minutes in D10 , 246.4± 25.7 minutes in D5 and 140.1 ± 32.3 minutes in Group N. Onset and regression of sensory and motor block were highly significant (N verses D5,N verses D10 and D5 verses D10).

They concluded that dexmedetomidine has a dose dependent effect on the onset and regression of sensory and motor block when used as an adjuvant to bupivacaine in spinal anaesthesia.

F A Khan et al [36] in 2006 conducted a study to evaluate and compare the characteristics of spinal block, its postoperative analgesic effects and its side effects using intrathecal bupivacaine with fentanyl or buprenorphine in elderly patients undergoing urological surgeries.

Sixty patients aged sixty and above scheduled for elective transurethral resection of prostate were divided into three groups of 20 each. Group L (control) received 2 ml of 0.75% bupivacaine. Group B received 2 ml of 0.75% bupivacaine with 30 µg buprenorphine. Group F received 2 ml of 0.75% bupivacaine with 10 µg fentanyl.

The mean time for the sensory block to reach T10 level was 3.2 ± 2 minutes in Group F and 4.3 ± 1 minute in Group B and 4.5 ± 2 minutes in

Group L. The duration of sensory block was significantly longer in Group B. Median block levels reached T8 in all groups. All patients required postoperative analgesia in Group L and F except six patients in buprenorphine group.

They concluded that buprenorphine 30 µg in combination with bupivacaine 0.75% 2 ml provided analgesia of comparable clinical onset and longer duration but was associated with a clinically increased incidence of nausea and vomiting in elderly patients.

G.E.Kanazi et al [14] **in 2005** conducted a prospective, double blind study in 60 patients undergoing transurethral resection of prostate or bladder tumour under spinal anaesthesia. The aim was to compare the onset and duration of sensory and motor block, hemodynamic changes and level of sedation following intrathecal administration of bupivacaine with either dexmedetomidine or clonidine.

60 patients were randomly allocated into 3 Groups. Group B received 12 mg of hyperbaric bupivacaine, Group D received 12 mg of bupivacaine of supplemented with 3µg of dexmedetomidine, Group C received 12 mg of bupivacaine supplemented with 30µg of clonidine.

The onset time to reach peak sensory and motor levels and the sensory and motor regression times were recorded. Haemodynamic changes and the level of sedation were also recorded. The mean time to reach T10 sensory block was 9.7 ± 4.2 minutes in Group B, 7.6 ± 4.4 minutes in Group C, 8.6 ± 3.7 in Group D. The mean time to reach peak sensory level was 20.2 ± 8.4 minutes in Group B, 18.7 ± 9.2 minutes in Group C, 24.5 ± 14.8 minutes in Group D. The mean time to reach Bromage 3 was 13.2 ± 5.6 in Group D, 11.7 ± 5.9 minutes in Group C, 20.7 ± 10.3 minutes in Group B. The mean values of MAP and heart rate were comparable between 3 Groups throughout the intra op and post-operative period. All patients had oxygen saturation > 96% at all times and did not require additional oxygen in PACU.

They concluded that supplementation of spinal Bupivacaine with low dose of intrathecal Dexmedetomidine or clonidine produces significantly shorter Onset of motor block and significantly longer sensory and motor block than bupivacaine alone. Dexmedetomidine 3µg and Clonidine 30µg have a equipotent effect on the characteristics of the block without any significant hemodynamic instability or sedation.

Talke et al [35] ***in 1997*** conducted a randomised double blind study in nine male volunteers .Dexmedetomidine was administered by computer controlled infusion, targeting its plasma concentration at 0.0,0.3,0.6 ng/ml. Each day skin

and core temperature were increased to provoke sweating and then subsequently reduced to elicit vasoconstriction and shivering. The dose dependant effects of dexmedetomidine on thermoregulatory response threshold were then determined using linear regression. Heart rate, blood pressure and plasma catecholamine levels were measured.

They concluded that dexmedetomidine markedly increased the range of temperature not trigerring thermoregulatory defence and it is likely to prove an effective treatment for shivering.

Capogna et al [11] **in 1988** conducted a double blind study to determine the effects of two doses of intrathecal Buprenorphine for post-operative pain relief in elderly patients. 90 patients aged 56 to 85 years scheduled for suprapubic prostatectomy were randomly divided into 3 groups of 30 each.

Group A received 30 mg of hyperbaric Bupivacaine. Group B received 30 mg hyperbaric Bupivacaine plus 0.03 mg of Buprenorphine. Group C received 30 mg hyperbaric bupivacaine + 0.045 mg of buprenorphine. The mean pain free interval was 103.45 minutes in Group A (control group),183.06 minutes in Group B, 430.16 minutes in Group C. In Group B pain increased gradually from 5 - 8 hours. In Group C pain increased from 7 - 12 hours. The mean respiratory rate in all 3 groups during the first12 hours remains stable. In

Group C respiratory rate transiently decreased below 10 breaths per minute in one patient, but no treatment was required.

Heart rate and blood pressure remained within the physiological range during the observational time. Nausea and vomiting occurred in 11 Patients who received 0.03 mg buprenorphine and in 14 patients who received the larger dose.

They concluded that intrathecal buprenorphine provided postoperative analgesia with minimal disturbance of consciousness, Comfortable breathing and reduced the risks of postoperative complications. Intrathecal administration of buprenorphine 0.03 mg or 0.045 mg may be used for postoperative analgesia in elderly patients. The higher concentration offers more prolonged analgesia without any further significant increase in side effects.

MATERIALS AND METHODS

Study design: Double blinded randomised case control study.

After obtaining approval from the institutional ethical committee, Thanjavur medical college, Thanjavur, the study was conducted in 60 ASA grade 1 or 2 patients undergoing elective lower abdominal surgeries like Hernia repair and appendicectomy under spinal anaesthesia. Before including the patients for the study, all patients were explained about the procedures and a written informed consent was obtained.

INCLUSION CRITERIA:

- Adult patients aged 18 - 60 years of either sex
- ASA 1 and 2 patients.
- Patients undergoing elective lower abdominal surgeries.

EXCLUSION CRITERIA:

- Patients with known contraindication for spinal anaesthesia.
- Patients with coagulation disorders or on anticoagulation therapy.

- Patients with cardiac disease, heart blocks and dysarrythmias
- Patients with betablockers & alpha antagonists.

PREOPERATIVE PREPARATION:

After routine preoperative assessment at the patients' waiting room in the OT, basal line readings of the vital parameters were recorded. Intravenous line started. The patients were randomly allocated into two groups of 30 each by using closed cover technique.

In the operating room, appropriate equipment for airway management and emergency drugs were kept ready. The horizontal position of the operating table was checked. Patients were shifted to the operating room and positioned.

Non-invasive blood pressure monitor, pulse oximeter and ECG leads were connected to the patient. Preoperative baseline systolic and diastolic blood pressure, mean arterial pressure, pulse rate, respiratory rate and oxygen saturation were recorded. Patients were preloaded with 10ml/kg of ringer lactate 15minutes prior to the subarachnoid block. On sitting position, the skin over the back was prepared with antiseptic solution and draped with sterile towel.

BD GROUP

- Patients received 3ml 0.5% bupivacaine (15mg)
- Dexmedetomidine (5µg) in 0.5 ml normal saline.

BB GROUP

- Patients received 3ml 0.5% bupivacaine(15mg)
- 0.5ml Buprenorphine (75µg)

Total volume of the injected solution was 3.5ml in both groups.

After skin's infiltration with 2% lidocaine, 25G Quincke's needle was inserted at the L3/4 interspace in the midline. After confirming free flow of CSF, the prepared solution was injected. The patients were made to lie supine immediately after injection and the time at which the spinal anaesthesia performed was noted.

The following parameters were noted.

- Time of injection of subarachnoid block.
- Time of onset of sensory block at T8 level.
- Time of onset of motor block.
- Duration of sensory block.
- Duration of motor block.
- Degree of sedation.
- Time for sensory regression to S1 dermatome.
- Duration of surgical procedure.

- Systolic and Diastolic blood pressure, Mean Arterial Blood pressure, pulse rate and oxygen saturation were recorded at 0, 3rd and 5th minute and thereafter every 5 minutes upto 45 minutes of the procedure.

- Hypotension was said to have occurred if the MAP fell less than 60 mmHg and treated with 100% O2, increasing the infusion rate of IV fluids and Inj. Ephedrine in incremental doses of 6mg at interval of 2 minutes.

- Bradycardia was defined as heart rate less than 50/min and was planned to be managed with intravenous atropine in incremental doses.
- Respiratory depression was said to be present if respiratory rate was less than 8/minute and / or Spo2 < 90%. It was planned to be managed with mask ventilation or intubation and IPPV.
- Any discomfort like nausea, vomiting, shivering, pruritus and adverse events such as hypotension, bradycardia respiratory depression and ECG changes were noted.
- Vomiting was planned to be managed with Inj.Ondansetron 4mg intravenously.
- On completion of surgery, patient was shifted to post anaesthesia care unit for observation. Patients were transferred to postoperative ward after complete resolution of motor blockade and stabilization of blood pressure.
- Vital signs and oxygen saturation were recorded until recovery of patients from anaesthesia.
- Injection Diclofenac sodium 75mg was given intramuscularly when the patient complained of pain in the postoperative period (rescue analgesic).

- Patients were followed up for one week postoperatively for headache, dysaesthesia in thighs, buttocks or lower limbs.

SENSORY BLOCK

The **onset** of sensory block was defined as the time between the injection of anaesthetic solution and the absence of pain at the T8 dermatome. Sensory block was assessed by loss of sensation to pin prick using 25G sterile needle bilaterally along the midclavicular line. This assessment started immediately after turning the patient to supine position and continued every minute till loss of sensation to pinprick at T8 level was noted.

The **duration** of sensory block was defined as the time between the intrathecal administration of anaesthetic solution and the first supplementation of rescue analgesic when patient complained of pain.

MOTOR BLOCK

Motor block was assessed bilaterally using Modified Bromage scale.

MODIFIED BROMAGE SCALE

0- No block. Able to raise extended legs against gravity.

1- Unable to raise extended legs, but just able to flex knees.

2- Unable to flex knees but able to flex ankles.

3- Total block. Inability to flex ankle/ move leg.

Assessment of motor block was started immediately after turning the patient to supine position and continued every minute till Bromage score of 3 was reached. The **onset** of motor block was defined as the time to achieve Bromage score of 3 from the time of intrathecal injection. **Duration** of motor block was taken as the time from intrathecal injection to return of Bromage score of 0 (complete recovery).

SEDATION

RAMSAY SEDATION SCORE was used to assess the degree of sedation.

1. Anxious and Agitated.
2. Cooperative, oriented, tranquil
3. Responds only to verbal commands
4. Asleep with brisk response to light stimulation
5. Asleep with sluggish response to light stimulation
6. Asleep without response to light stimulation

DURATION OF ANALGESIA

The duration of effective analgesia was defined as the period from spinal injection to the first occasion when the patient complaints of pain in the postoperative period.

OBSERVATION AND ANALYSIS

All 60 patients in two groups completed the study without any exclusion. Inter group analysis was done and the results were as followed.

The collected data were analysed by chi square test and results obtained in the form of range, mean and standard deviation. The probability value ‘p’ of less than 0.05 considered statistically significant.

Patient demographic data that includes age, sex, and duration of surgery between two groups were comparable.

Table 1: Age distribution

Age group	Age in years			
	Group BB		Group BD	
	No.	%	No.	%
Below 30 years	6	20	8	26.7
31 – 40	9	30	6	20
41 – 50	6	20	9	30
Above 50	9	30	7	23.3
Total	30	100	30	100
Range	19 – 60 years		18 – 60 years	
Mean	42.33		40.57	
SD	12.88		13.22	
'p' value	0.875 Not significant			

The age distribution was in the range of 19-60 in Group BB and 18-60 in Group BD. The 'p' value for mean age was not statistically significant (p value = 0.875).

AGE DISTRIBUTION

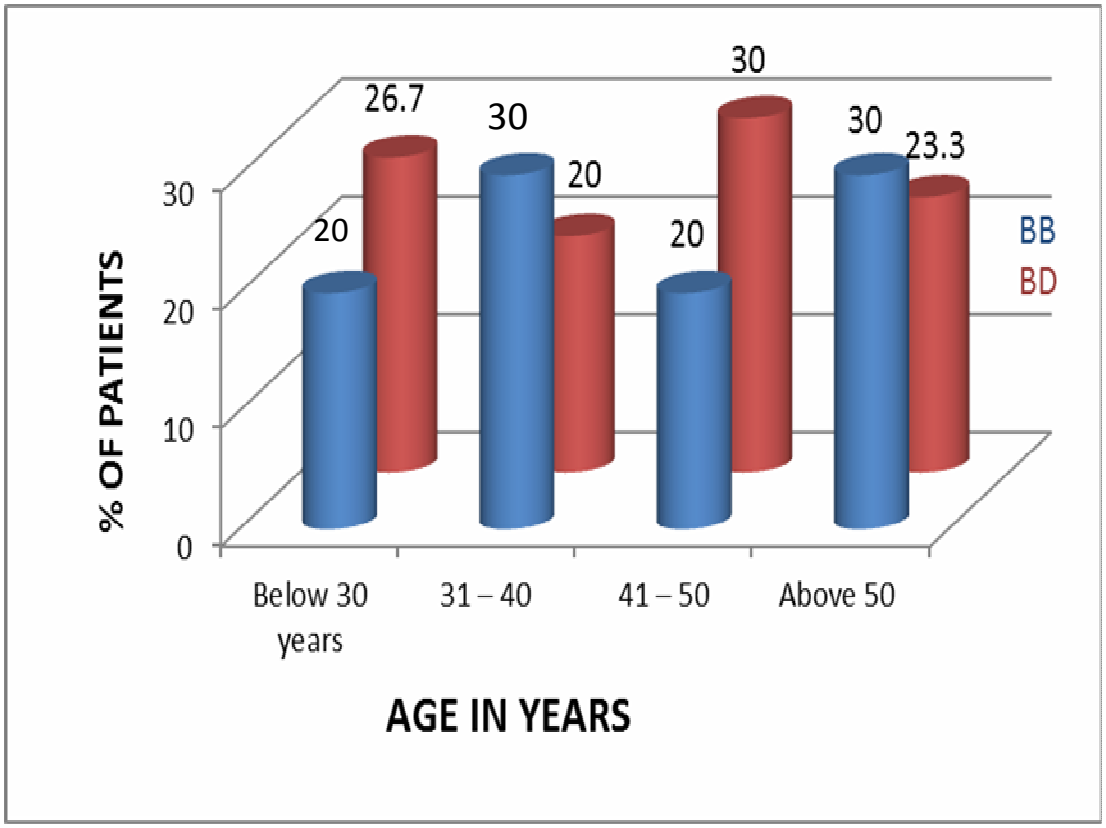
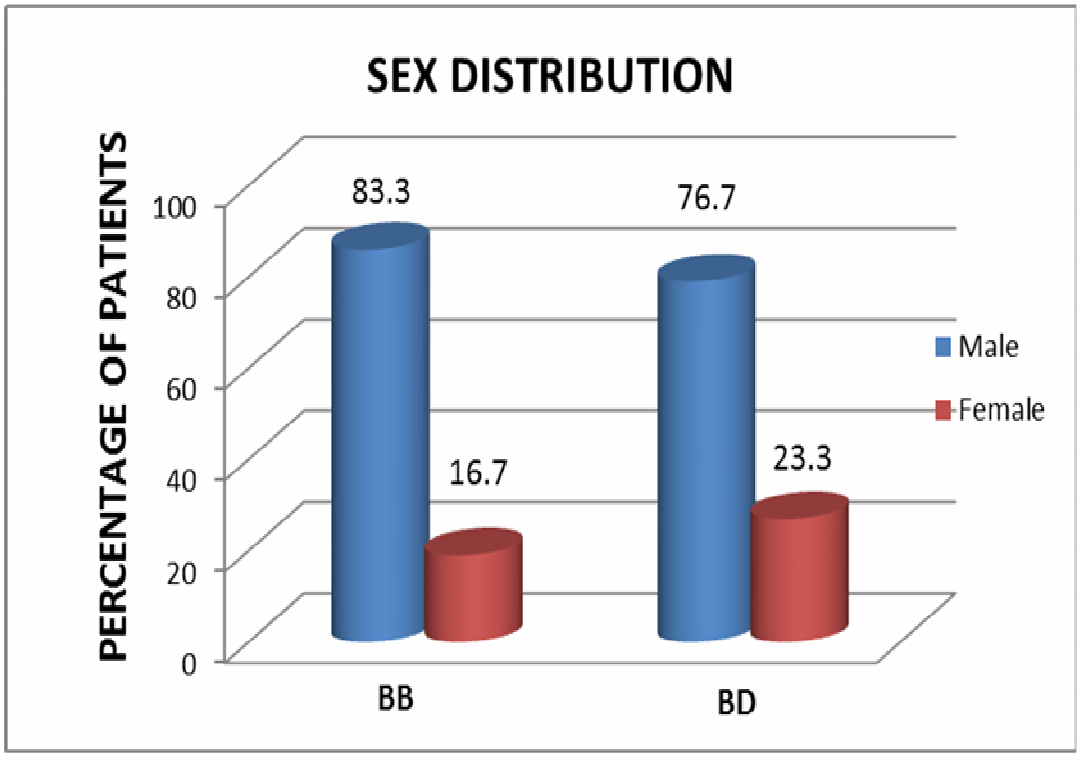


Table 2: Sex distribution

Sex	Group BB		Group BD	
	No	**%**	**No**	**%**
Male	25	83.3	23	76.7
Female	5	16.7	7	23.3
Total	30	100	30	100
'p'	0.752 Not significant			

Though male and female ratio is not equal in either group, statistics between the groups for sex distribution was not significant. The p value is 0.752.


SEX DISTRIBUTION
PERCENTAGE OF PATIENTS
100
80
60
40
20
0
83.3
16.7
76.7
23.3
BB
BD
Male
Female

EFFICACY OF THE TWO DRUGS

Table 3: Time of onset of sensory block

Parameter	Time of onset of sensory block (in minutes)	
	Group BB	**Group BD**
Range	3-4	2-3
Mean	3.47	2.57
SD	0.507	0.504
'p' value	0. 629 Not Significant	

The time of onset of sensory block was slower in Group BB (3.47± 0.507) when compared with Group BD (2.57± 0.504) and the p value was statistically not significant (0.629 > 0.05).

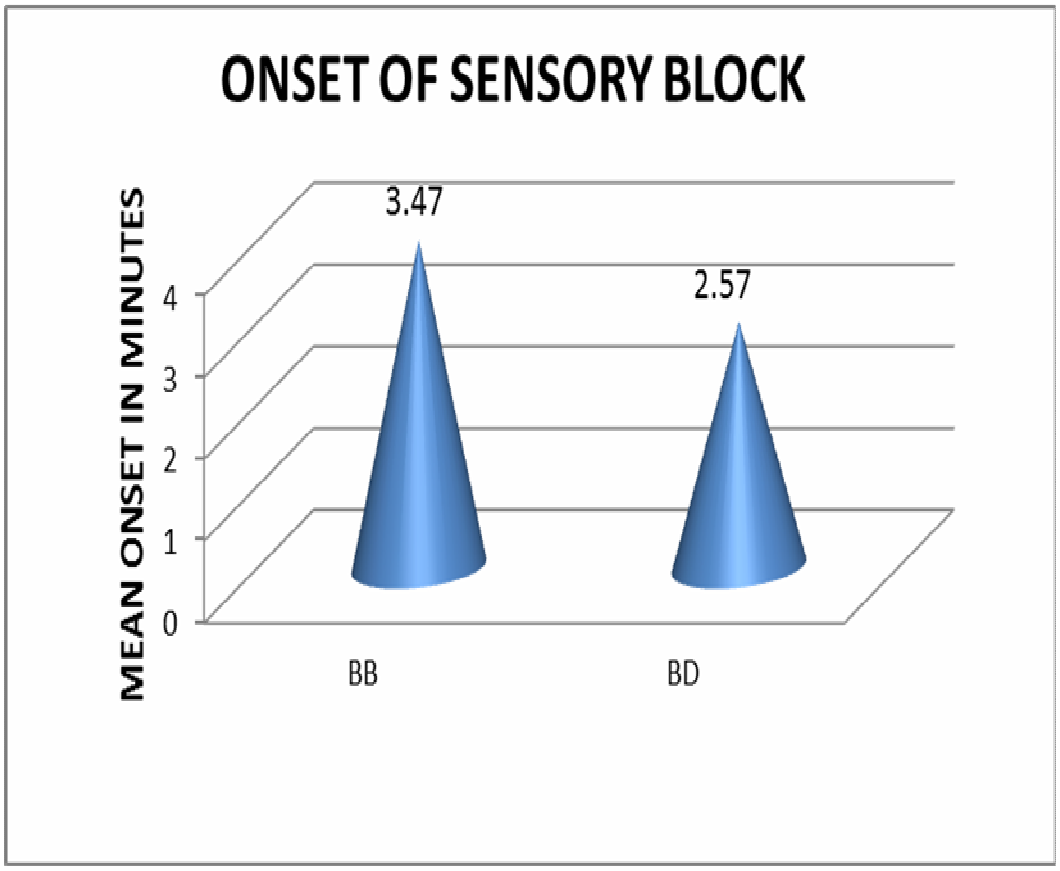

ONSET OF SENSORY BLOCK
MEAN ONSET IN MINUTES
0
1
2
3
4
3.47
2.57
BB
BD

Table 4: Time of onset of motor block

Parameter	Time of onset of motor block (in minutes)	
	Group BB	**Group BD**
Range	3-5	3-5
Mean	3.83	4.13
SD	0.817	0.78
'p' value	0. 775 Not Significant	

The average time taken for the onset of motor block was 3.83 minutes in Group BB and 4.13 minutes in Group BD. It was statistically not significant (p value 0.775 > 0.05).

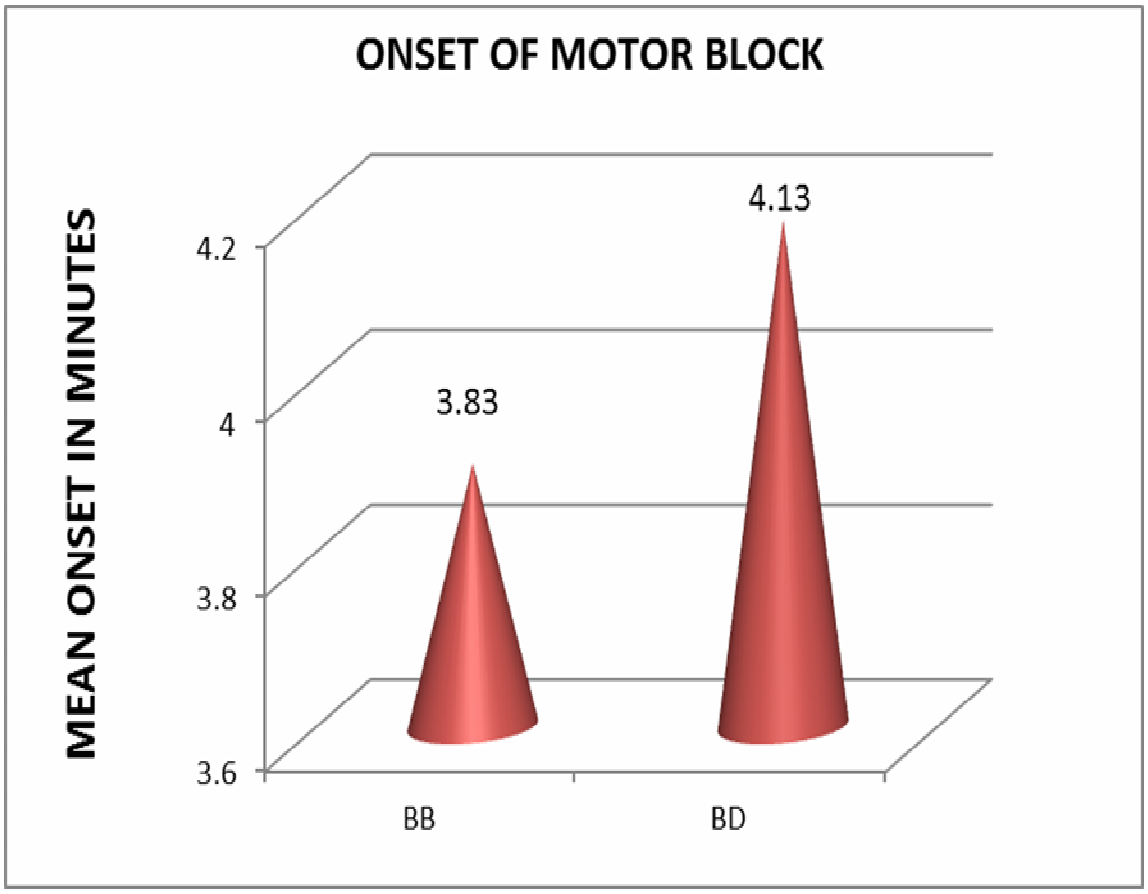

ONSET OF MOTOR BLOCK
MEAN ONSET IN MINUTES
4.2
4
3.8
3.6
3.83
4.13
BB
BD

Table 5: Duration of Sensory block

Parameter	Duration of Sensory block (in minutes)	
	Group BB	**Group BD**
Range	303-360	480 – 520
Mean	332	502.13
SD	18.81	12.27
'p' value	0. 005 Significant	

The mean duration of sensory block was shorter in Group BB (332 ± 18.81) when compared with Group BD (502.13 ± 12.27). It was statistically significant (p value= 0.00 < 0.05). The mean duration of sensory block in Group **BD** is approximately ***51% longer*** than Group BB.

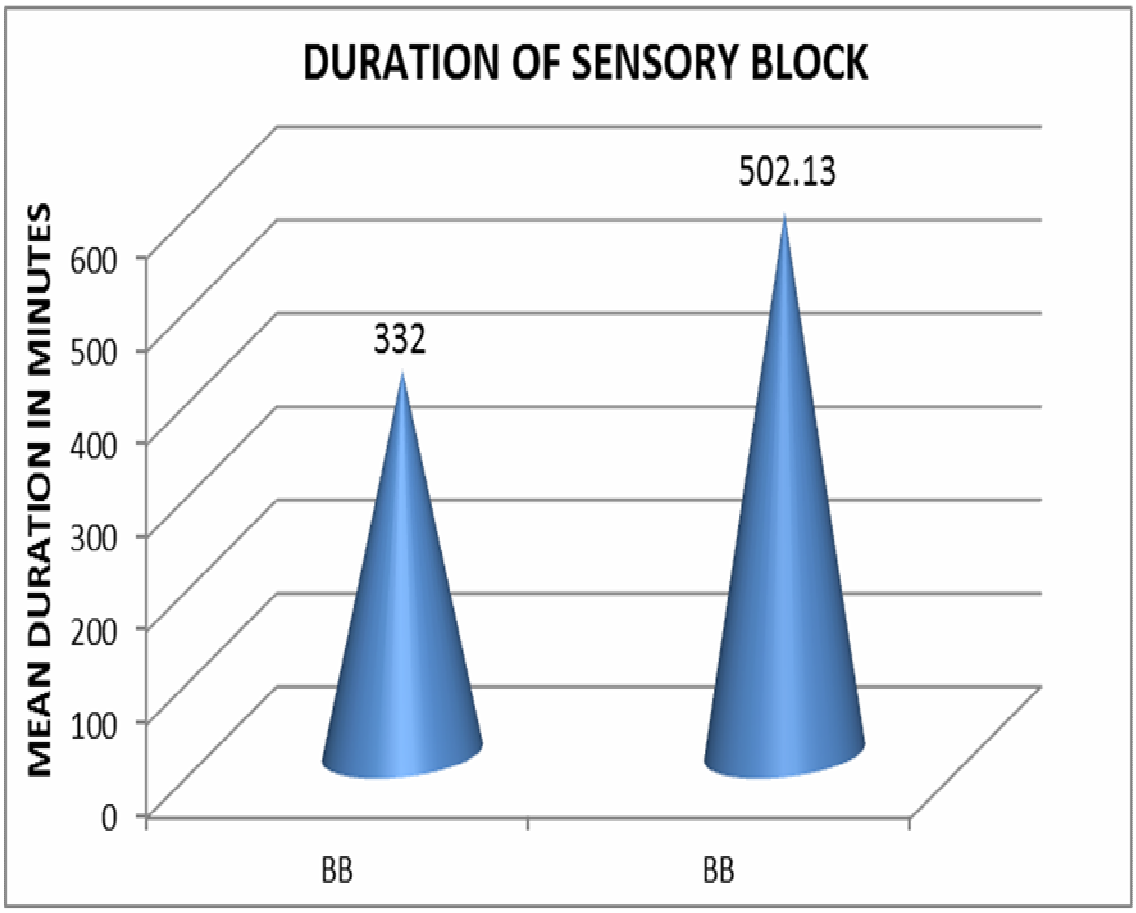

DURATION OF SENSORY BLOCK
MEAN DURATION IN MINUTES
600
500
400
300
200
100
0
332
502.13
BB
BB

Table 6: Duration of motor block

Parameter	Duration of motor block (in minutes)	
	Group BB	**Group BD**
Range	293-360	413-460
Mean	298.63	432.33
SD	35.79	12.74
'p' value	0. 000 Significant	

The mean duration of motor block was shorter in Group BB (298.63 ± 35.79) when compared with Group BD (432.33 ± 12.74). It was statistically significant (p value = 0.00 < 0.05). The mean duration of motor block in Group **BD** is about approximately ***44% longer*** than Group BB.

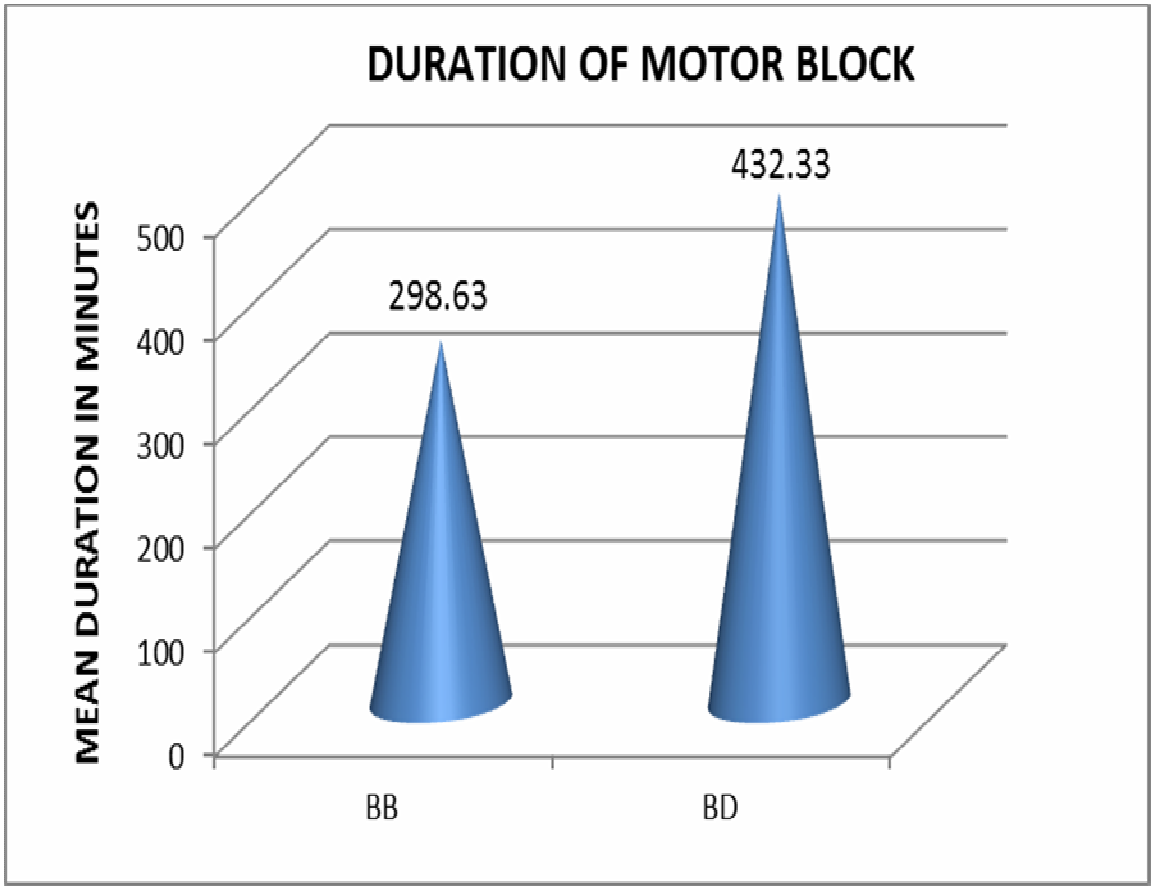
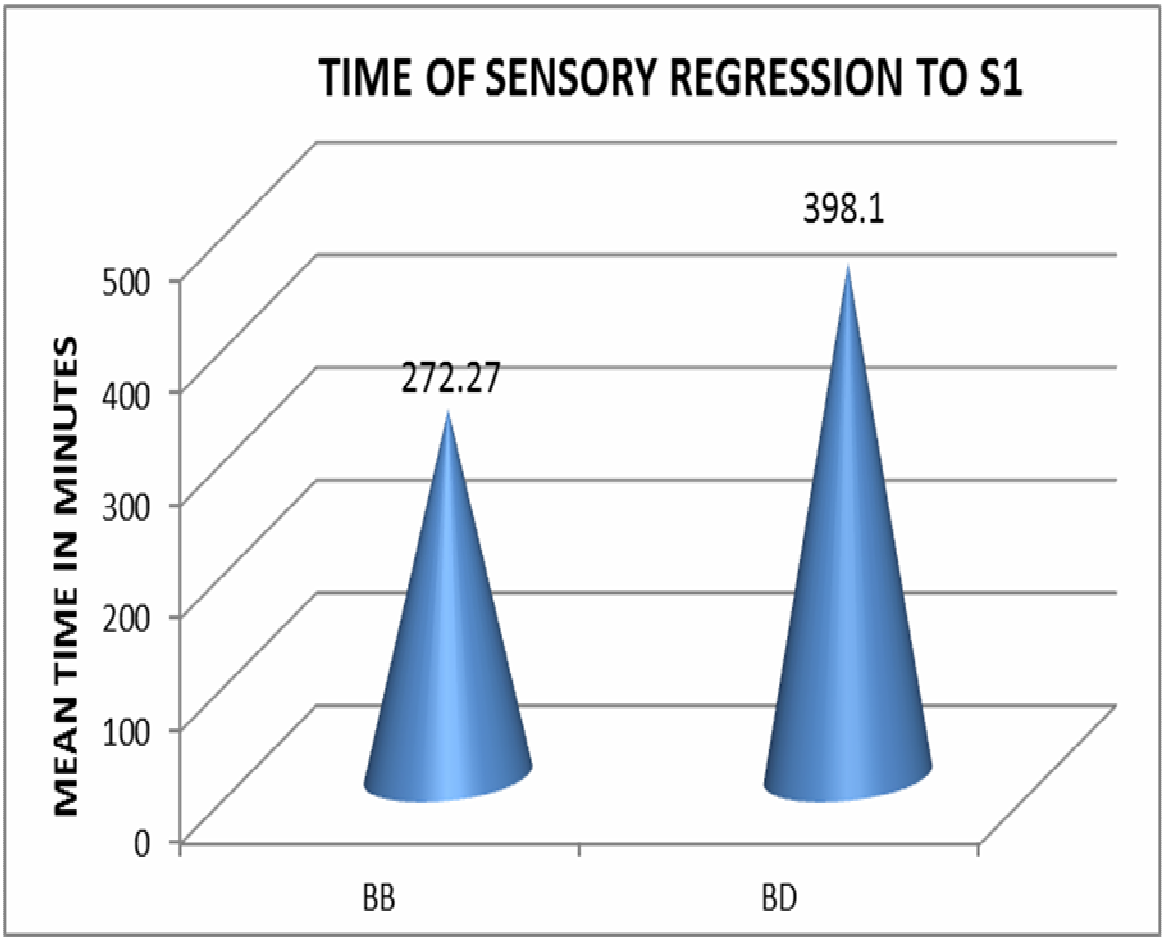

DURATION OF MOTOR BLOCK
MEAN DURATION IN MINUTES
500
400
300
200
100
0
298.63
432.33
BB
BD

Table 7: Time of sensory regression to S1

Parameter	Time of sensory regression to S1 (in minutes)	
	Group BB	**Group BD**
Range	250-299	389-409
Mean	272.27	398.1
SD	15.39	6.50
'p' value	0. 001 Significant	

The time of sensory regression to S1 was shorter in Group BB (272.27 ± 15.39) when compared with Group BD (398.1 ± 6.50). It was statistically significant (p value = 0.048 < 0.05). There was a delay in sensory regression of approximately 1/3 times (30%) in Group **BD** comparing to Group BB.


TIME OF SENSORY REGRESSION TO S1
MEAN TIME IN MINUTES
500
400
300
200
100
0
272.27
398.1
BB
BD

HAEMODYNAMIC VARIABLES

Table 8: Mean arterial Pressure

Time Interval	BB Group (Mean ± SD)	BD Group (Mean ± SD)	P value
0 min	81.23 ± 10.45	80.17 ± 10.45	0.963
3 min	80.57 ± 13.35	80.90 ± 10.47	0.089
5 min	75.63 ± 14.47	80.33 ± 13.79	0.854
10 min	78.60 ± 13.71	83.20 ± 12.63	0.897
15 min	75.07 ± 11.96	78.97 ± 12.75	0.337
20 min	81.17 ± 13.09	79.53 ± 13.21	0.780
25 min	79.60 ± 10.83	79.60 ± 10.61	0.958
30 min	74.50 ± 10.86	76.97 ± 11.53	0.406
35 min	82.13 ± 12.96	83.47 ± 11.56	0.222
40 min	77.60 ± 10.93	76.43 ± 11.08	0.663
45 min	78.43 ± 11.50	77.57 ± 12.10	0.503

The mean arterial pressure was monitored from preoperative basal to 45th minute of the procedure (11 intervals). None of the intervals had statistical significance.

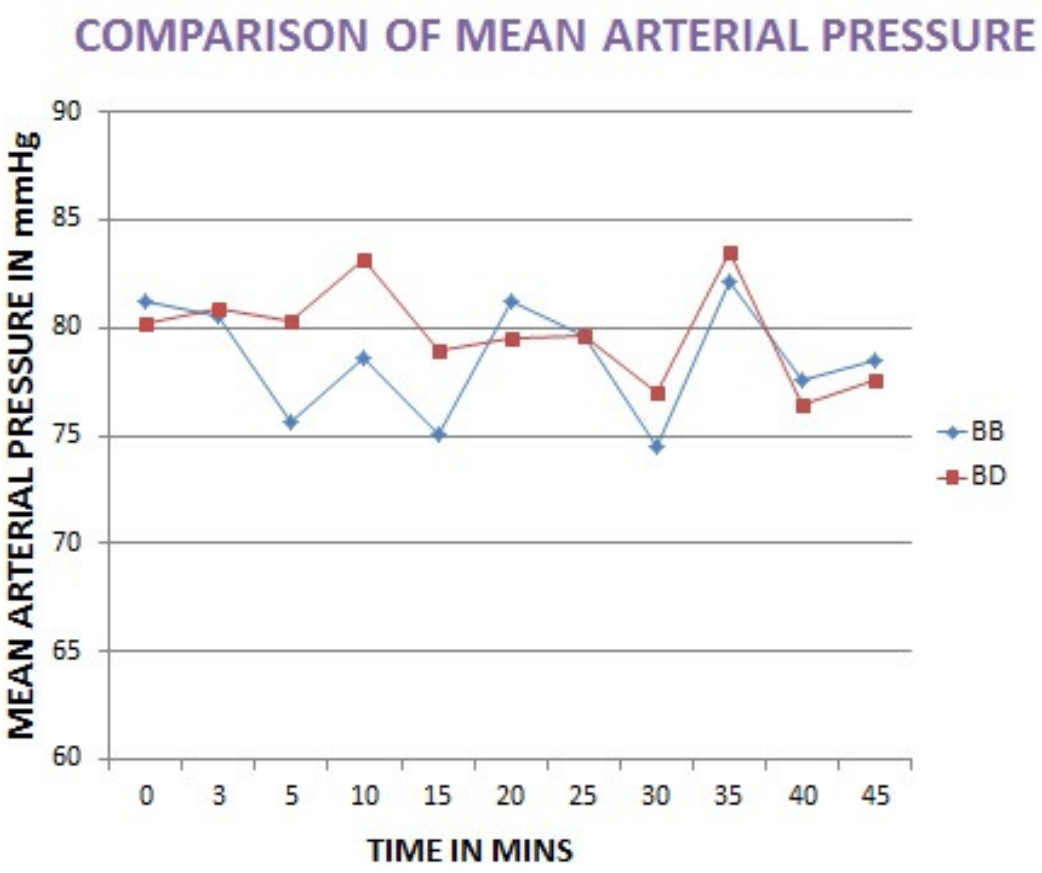

COMPARISON OF MEAN ARTERIAL PRESSURE
MEAN ARTERIAL PRESSURE IN mmHg
90
85
80
75
70
65
60
0
3
5
10
15
20
25
30
35
40
45
TIME IN MINS
BB
BD

Table 9: Heart rate

Time Interval	BB Group (Mean ± SD)	BD Group (Mean ± SD)	P value
0 min	78.93 ± 12.21	77.43 ± 9.16	0.035*
3 min	81.47 ± 13.37	74.27 ± 9.13	0.000*
5 min	80.63 ± 12.79	81.07 ± 11.55	0.360
10 min	78.37 ± 13.96	80.33 ± 11.89	0.769
15 min	77.73 ± 15.92	77.80 ± 12.18	0.083
20 min	79.23 ± 13.13	82.40 ± 13.49	0.806
25 min	79.77 ± 12.05	78.57 ± 12.43	0.668
30 min	80.93 ± 12.50	79.87 ± 12.58	0.684
35 min	79.90 ± 11.72	78.17 ± 11.21	0.584
40 min	79.70 ± 12.15	80.73 ± 11.36	0.442
45 min	77.23 ± 11.98	76.37 ± 11.98	0.874

In this study, heart rate less than 50 beats was considered as bradycardia while collecting the data. Heart rate was recorded in 11 intervals, out of which only 2 intervals (0 and 3rd minute) were statistically significant (*).

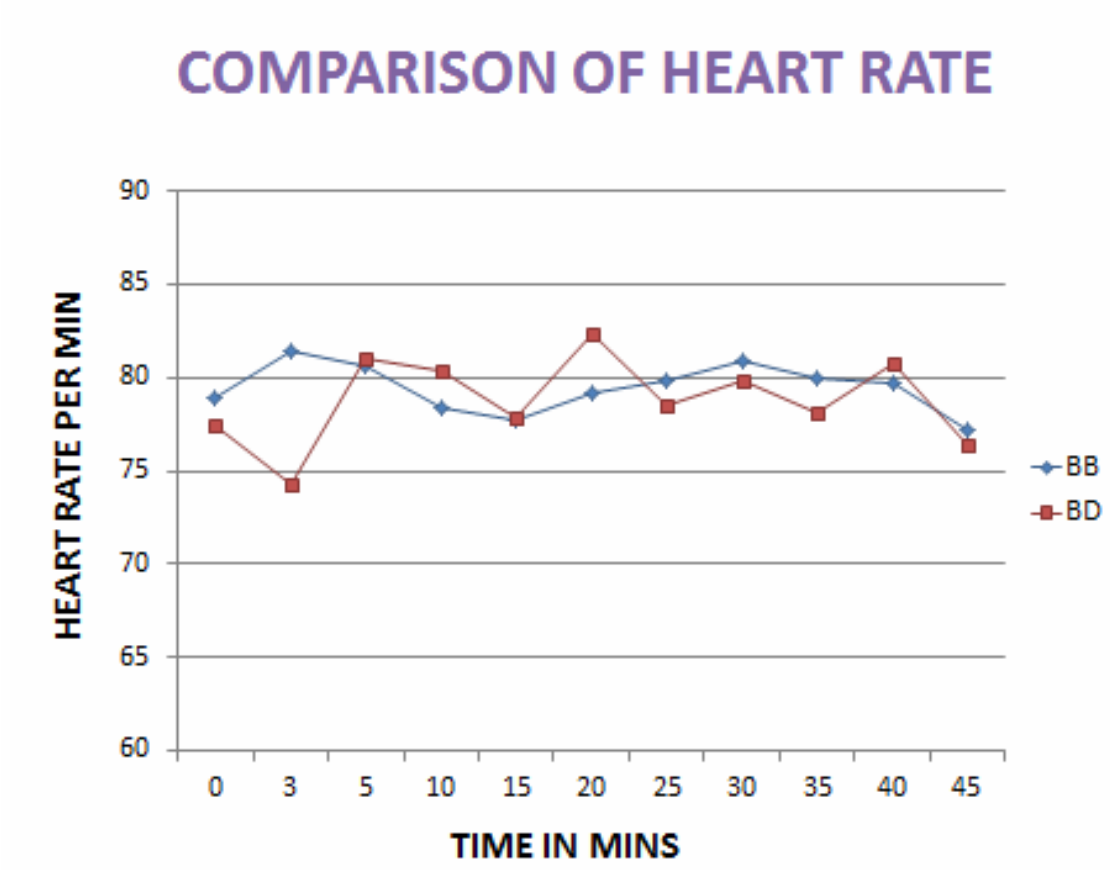

COMPARISON OF HEART RATE
HEART RATE PER MIN
90
85
80
75
70
65
60
0
3
5
10
15
20
25
30
35
40
45
TIME IN MINS
BB
BD

Table 10: SPO2

Parameter	SPO2	
	Group BB	**Group BD**
Range	97-100%	97-100%
Mean	98.53	98.43
SD	1.008	1.006
'p' value	0.972 Not significant	

Oxygen saturation was in the range of 97 – 100 %. It was not statistically significant (p value 0.972 > 0.05).

Table 11: Degree of Sedation

Parameter	Degree of Sedation (Ramsay sedation scale)	
	Group BB	**Group BD**
Range	1-3	2-3
Mean	1.83	2.40
SD	0.791	0.498
'p' value	0. 018 Significant	

In table 11, Degree of Sedation in the two groups was depicted. 'p' value was statistically significant (0. 018 < 0.05). Degree of Sedation was **better** in Group BD when compared with Group BB.

Table 12: Adverse effects

Adverse effects	Group BB		Group BD	
	No	%	No	%
Hypotension	8	27	0	0
Bradycardia	6	20	2	7
Shivering	3	10	0	0
Nausea &Vomiting	3	10	0	0
Total cases with adverse effects	20*	67	2	7
Total cases without adverse effects	10*	23	28*	93
Total	30*	100	30*	100

* More than one adverse effect was present in one case in each group

In Group BB, 8 patients (27%) had hypotension and received ephedrine. In Group BD, none of the patients had hypotension as an event. But these episodes were not statistically significant (**refer to table 8**). Other adverse effects between the two groups were comparable.

DISCUSSION

Subarachnoid block with bupivacaine has been most extensively used for lower abdominal surgeries because of its simplicity, speed, reliability and minimal exposure to depressant drugs. However, a single intrathecal injection of bupivacaine alone provides analgesia for only 2 – 2.5 hours. Most patients require further analgesia during post operative period.

This double blinded, prospective, randomised study was conducted in Thanjavur medical college, Thanjavur with an aim to compare the effects of intrathecal Dexmedetomidine and Buprenorphine as an adjuvant to 0.5% hyperbaric bupivacaine.

The study included 60 patients belonging to the age group of 18-60 years of both sexes of ASA grade 1 and 2 scheduled to undergo elective lower abdominal surgeries.

One of the study drugs, Buprenorphine, a highly lipophilic and centrally acting partial opioid agonist has rapid onset of action following intrathecal administration. It has been found recently that prolonged duration of action of buprenorphine is due to its local anaesthetic action [37]. The lesser side effects in the post-operative period were due to its high lipid solubility [38].

Because of its high lipophilic nature, it diffuses quickly into the neural tissue and decreases the chance of rostral spread.

Another drug in the study, Dexmedetomidine which is a specific α2 adrenergic agonist, being used in recent times as an additive to intrathecal hyperbaric bupivacaine to prolong the quality and duration of analgesia. The mechanism for the prolongation of the duration of sensory and motor blockade produced by local anaesthetic is *not clearly known* [33]. It is attributed that α 2 adrenergic agonist (Dexmedetomidine) acts by binding to post synaptic dorsal horn neurons and to the C- fibres in the pre synaptic region. The prolonged analgesic action of intrathecal α2 agonist is by decreasing the release of C-fibres neurotransmitters and by causing hyperpolarisation of neurons in the post synaptic dorsal horn [39].

Even though there are lot of adjuvants, the above mentioned two adjuvants were considered for this study because there were only very few studies in the literature comparing the benefits and side effects of buprenorphine and dexmedetomidine as an adjuvants to bupivacaine for lower abdominal surgeries [27]. Also, they are pharmacologically different drugs but their effects are similar in terms of hemodynamic stability, onset of sensory and motor block and adverse effects [27].

But these two drugs differ in the clinical effects especially in the duration of sensory and motor block, sensory regression and degree of sedation[27] .

Kanazi GE et al [14] have used 3 µg dexmedetomidine in their study and said to have comparable equipotent effect with clonidine. Hala EA Eid et al [29] studied the effects of dexmedetomidine on a dose related manner (control, 10 µg and 15µg) and confirmed the prolongation of duration of analgesia. Many studies have chosen 5µg of dexmedetomidine as an additive to intrathecal hyperbaric bupivacaine and proven efficacy *[9,30]*. Hence in our study we chose 5µg dexmedetomidine as an additive to hyperbaric bupivacaine.

Few studies have been conducted with a higher dosage of buprenorphine. C**apogna et al [11]**, **Mahima gupta et al [27] and sapkal Praveen S et al [34],** have chosen 60µg of buprenorphine as an additive to intrathecal bupivacaine and showed to have a significant prolonged duration of analgesia along with nausea and vomiting that were not statistically significant.

Mahima gupta et al[27] also shown the duration of sensory blockade was 289.6 minutes in buprenorphine group and 493.6 minutes in dexmedetomidine group.

In this study, 75µg of buprenorphine was used instead of 60µg to evaluate whether the increased dosage of 15µg buprenorphine would help in further prolongation of duration of analgesia with a minimal side effects (PONV).

The results of the clinical study are discussed under the following headings.

Onset of sensory and motor block.

Duration of sensory block.

Duration of motor block.

Time for sensory regression to S1

Hemodynamic stability and

Adverse effects.

ONSET OF SENSORY AND MOTOR BLOCK

The mean onset of sensory block in buprenorphine group was 3.47 minutes whereas in dexmedetomidine group it was 2.57 minutes. It was not statistically significant.

The mean onset of motor block in buprenorphine group was 3.83 minutes whereas in dexmedetomidine group, 4.13 minutes. It was not statistically significant.

Though the values of onset of motor blockade is similar to ***Mahima gupta et al***[27] and others, the onset of sensory blockade of dexmedetomidine group was clinically faster than buprenorphine group in our study which could not be explained.

DURATION OF ANALGESIA

Duration of analgesia was taken from the time of intrathecal injection of drugs to the first supplementation of rescue analgesic when patient complained of pain. In our study, the mean duration of analgesia was 332 minutes in buprenorphine group and 502.13 minutes in dexmedetomidine group.

The duration of analgesia in the **Buprenorpine** Group was 332 minutes whereas in the study conducted by ***Mahima gupta et al***[27] it was 289.66 ±

68.94. The prolongation of duration in our study could be explained by the dosage difference of buprenorphine (75 µg **Vs** 60µg). But the mean duration of analgesia in the studies conducted by ***Shaikh and Kiran et al***[8] ***and Capogna et al*** [11]was 475 minutes and 430 minutes respectively which is very high than our study. This gross difference might be explained by the geriatric group of patients in Capogna et al and lower limb surgeries included in Safiya et al as noted by Mahima gupta et al.

The duration of analgesia in the **dexmedetomidine** group in the study conducted by ***Mahima gupta et al***[27] was 493 minutes and the study conducted by ***Shah et al***[33] was 474 minutes. The duration of analgesia was significantly prolonged in the study done by ***Rajni Gupta et al***[9] (478 minutes). In our study, the mean duration of analgesia was 502.13 minutes in dexmedetomidine group which was similar to above mentioned studies. Also, the study done by ***Eid et at al***[29] showed that duration of analgesia with dexmedetomidine Group was proportional to its dose.

In this study, Dexmedetomidine group had prolonged duration of analgesia compared to Buprenorphine group which was 51% higher than the later. ***Mahima Gupta et al*** [27] have shown similar results. The prolonged analgesic action of intrathecal α2 agonist is by decreasing the release of C-

fibres neurotransmitters and by causing hyperpolarisation of neurons in the post synaptic dorsal horn [39].

DURATION OF MOTOR BLOCK

The duration of motor block was taken from time of intrathecal drug administration to the time taken to attain modified bromage 3. The mean duration of motor block in Buprenorpine group was 298.6 minutes and in dexmedetomidine group was 432.33 minutes (p value 0.00).

This was similar with the study conducted by ***Mahima gupta et al*** [27] **,** where the duration of motor block in *dexmedetomidine group* was 413.4 minutes and the study conducted by ***Rajni Gupta et al***[9] **,** where the duration of motor block was 421 minutes.

The mean duration of motor block in *buprenorphine group* is 298.6 minutes, whereas the duration of motor block in ***Mahima gupta et al*** [27] study was 205.17 minutes which is significantly lower than our study. This could be explained by the increased dosage used in our study.

In our study itself, motor blockade in dexmedetomidine group was about **45%** prolonged than Buprenorpine group. Such a prolongation of motor blockade may not be liked by many patients who have undergone surgeries that

would end by one hour. In this perspective, Buprenorphine would be a better adjuvant. Also, the duration of 'pure' sensory blockade (after the wear of motor blockade effect) in dexmedetomidine group was twice that of buprenorphine group (70 **Vs** 34 minutes). Still, Dexmedetomidine is a better drug as it would spare the rescue analgesic requirements.

TIME FOR SENSORY REGRESSION TO S1

The mean duration for sensory regression to S1 in buprenorphine group was 272.27 minutes and in dexmedetomidine group, 398.1 minutes.

In a study conducted by ***Mahima gupta et al*** [27], the mean duration for sensory regression to S1 in buprenorphine group was 225.9 min which was lower than the same group in our study. But in dexmedetomidine group it was 451.4 min that was higher than the same group in our study.

Subhi M Al-ghanem et al[31] showed that the mean duration for sensory regression to S1 dermatome was 274.8 minutes in dexmedetomidine group which was lower than our study. This may be because of the higher volume (3 ml) of a hyperbaric solution probably prolonged the regression time comparing to the lower volume (2ml) of isobaric solution in their study.

Rajni gupta et al [9] have shown that the mean time for sensory regression to S1 was 476 min in dexmedetomidine group which is higher than our study. This may be because either the usage of higher concentration(0.75%) of isobaric ropivacaine or due to the potentiation of intrathecal ropivacaine by intrathecal dexmedetomidine[40].

S1 dermatome is used as the sensory regression point in most of the studies [9, 27]. S1dermatome is well below the dermatomes those are involved in the surgery (T8 – L1) in our study. But patients in both groups ***never complaint of pain*** at the time of sensory regression to S1. More than that, analgesia was extended to the time for first analgesic requirement. This is the classical effect of adding an adjuvant to the local anesthetics i.e improving patients' comfortness and reducing both the postoperative analgesic requirement and side effects.

In this purview, in our study dexmedetomidine is superior to buprenorphine in having prolonged duration of sensory block, duration of motor block and sensory regression to S1.

HAEMODYNAMIC STABILTY

Al-Ghanem et al[31] in their study noted that the use of intrathecal dexmedetomidine to be associated with decrease in blood pressure and heart rate.

In the present study, it was noted 2 cases of bradycardia and nil cases of hypotension in dexmedetomidine group whereas 6 cases of bradycardia and 8 cases of hypotension in buprenorphine group. They were managed successfully with the use of atropine 0.6 mg I.V and ephedrine in incremental doses of 6 mg.

Bradycardia at 0 and 3 minute interval in dexmedetomidine group had the statistical significance.

Mahima gupta et al [27]in their studies also incidence of bradycardia was more in dexmedetomidine group. Dexmedetomidine causes bradycardia but the effect is more prominent when administered intravenously and with a higher dose[44].

DEGREE OF SEDATION

There were significant differences between the two groups with respect to the degree of sedation as evidenced by the significance value obtained from the chi square test that was less than 0.05. The need for further intraoperative sedation was nil in dexmedetomidine group.

Mahima gupta et al[27] in their study noted that the sedation score was higher in patients belonging to dexmedetomidine group as compared to buprenorphine group which is similar to our study. This was due to the action of dexmedetomidine on α2 receptors on locus ceruleus.

ADVERSE EVENTS

The incidence of nausea and vomiting were more in buprenorphine group as compared to dexmedetomidine group which is similar to the study conducted by ***Mahima gupta et al*** [27]. ***Capogna et al***[11] also observed more number of nausea and vomiting in buprenorphine group. Similar observations were seen by ***sapkal et al***[34]**.**

Talke et al[35] in their study observed that α_2 adrenergic agents have anti shivering property. In the present study we have not encountered any case of

shivering. This is in contrast to ***Mahima gupta et al***[27] study where the incidence of shivering was more in dexmedetomidine group when compared to buprenorphine group.

In the present study the SPO_2 was in the range of 97 – 100 % without oxygen supplementation. No incidence of respiratory depression, pruritus and ECG changes were found in both the groups.

SUMMARY

A clinical study was undertaken to compare the effects of intrathecal Buprenorphine and dexmedetomidine as additives to 0.5 % hyperbaric bupivacaine for spinal anaesthesia. This prospective, randomized, Double blind study was conducted on 60 adult patients of ASA physical status 1 and 2 in the age group of 18 to 60 years, posted for elective lower abdominal surgeries at Thanjavur Medical college Hospital, Thanjavur from the period June 2012 – July 2014.

Patients were randomly allocated into two groups namely, Group BB and Group BD of 30 each.

Patients in Group BB received 75mcg of Buprenorphine with 0.5% bupivacaine 15mg intrathecally.

Patients in Group BD received 5mcg of Dexmedetomidine with 0.5% bupivacaine 15mg intrathecally.

After connecting monitors, the required preloading done to all patients. Subarachnoid block was carried out under aseptic precautions. Pulse rate,

respiratory rate, arterial blood pressure and oxygen saturation were recorded at 0, 3, 5 minutes and thereafter every 5minutes up to 45 minutes intraoperatively.

The following parameters were observed - onset and duration of sensory block and motor block, time for sensory regression to S1, degree of sedation, hemodynamic stability and any side effects associated with these drugs.

Collected data were analysed using appropriate statistics.

Demographic datas were not statistically significant. The onsets of sensory and motor blockades were not statistically significant. The *duration* of sensory blockade was prolonged in *dexmedetomidine* group (**51%**) compared to buprenorphine group that was similar to ***Mahima gupta et al*** [27]. The Motor blockade, sensory regression to S1 were also got prolonged in Dexmedetomidine group which was also proven by ***Rajni gupta et al*** [9]. The degree of sedation was better in dexmedetomidine group than buprenorphine group.

(Ramsay sedation score of 3). Hemodynamic parameters were comparable between the groups.

CONCLUSION

The present study concludes that

1. The **onsets** of sensory and motor blockades were not statistically significance between the groups.

2. The **duration** of both sensory and motor blockades were prolonged in ***dexmedetomidine*** group compared to buprenorphine group with the best statistical significance.

3. Both groups had stable and comparable hemodynamics during the study.

4. Compared to buprenorphine, intrathecal administration of dexmedetomidine as additive to hyperbaric bupivacaine was associated with fewer side effects.

5. The degree of sedation was better in the dexmedetomidine group when compared to buprenorphine group.

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PROFORMA

Name	:	IP no	:
Age	:	Diagnosis	:
Sex	:	Procedure	:
Weight	:	ASA physical status	:
MPG	:	Duration of surgery	:

PREOPERATIVE OBSERVATIONS:

GENERAL PHYSICAL EXAMINATION		**SYSTEMIC EXAMINATION**	
Pulse rate	:	CVS	:
Bp	:	RS	:
Spo2	:		

GROUP **:** D/B

Position & site of injection :

Time of intrathecal injection of drug :

Time of onset of sensory block (min) :

Time of onset of motor block (min) :

Time for modified bromage 0(min) :

Duration of analgesia (min) :

Time for sensory regression to s1 dermatome :

Degree of sedation (<3/>3) :

Pre OP	10 min post spinal anaesthesia	Post OP

INTRAOPERATIVE HEMODYNAMIC CHANGES:

PARAMETERS	**0min**	**3min**	**5min**	**10 min**	**15 min**	**20 min**	**25 min**	**30 min**	**35 min**	**40 min**	**45 min**
H.R											
SBP											
DBP											
MAP											
SPO2											

SIDE EFFECTS AND COMPLICATIONS:

Nausea/vomiting :

Shivering :

Ephedrine required :

Atropine required :

Post op headache/back pain

S No	Name	Age(years)	Sex	ASA	Group	Duration of the surgery (min)	Surgery	Time of onset of Sensory Block(min)	Time of onset of motor Block(min)	Duration of sensory block(min)	Duration of motor block(min)	Time of sensory regression to S1(min)	HR(per min)												Mean arterial pressure (mm of Hg)												SPO2(%)												Sedation score			Adverse effects
													0	3	5	10	15	20	25	30	35	40	45	0	3	5	10	15	20	25	30	35	40	45	0	3	5	10	15	20	25	30	35	40	45	Pre Op	10 min after spinal anaesthesia	Post Op	
1	Meenakshi sundaram	44	M	I	BB	119	Appendicectomy	4	5	345	298	251	68	88	96	74	61	78	99	65	94	78	81	67	98	66	99	66	94	81	98	76	79	97	100	98	98	99	99	97	98	97	98	100	97	1	3	2	
2	Nallamuthu	60	M	I	BB	115	Hernioplasty	4	3	303	267	279	79	63	73	95	49	68	64	92	87	96	70	98	89	55	81	76	67	73	74	64	72	69	97	100	99	100	97	100	98	97	97	97	99	1	2	2	Bradycardia,Hypotension
3	Seetha	55	F	I	BB	92	Hernioplasty	4	3	327	323	250	60	89	85	64	93	92	75	93	76	74	67	76	65	90	95	77	60	95	68	90	98	75	100	99	97	100	97	100	97	98	100	99	99	1	2	3	Shivering
4	Ganesh	29	M	I	BB	103	Appendicectomy	3	4	338	334	277	76	65	93	93	62	94	95	81	86	78	60	70	63	66	82	89	77	70	70	86	77	71	98	100	98	98	98	99	97	98	100	100	99	2	3	2	
5	Ponnusamy	57	M	I	BB	98	Hernioplasty	3	4	350	359	257	91	99	68	88	81	82	76	99	65	70	81	79	66	83	84	94	69	90	75	85	65	75	98	98	97	100	97	97	100	99	100	100	99	2	3	3	vomiting
6	Jeyaraman	55	M	I	BB	99	Hernioplasty	4	5	319	354	261	84	61	65	73	90	89	63	92	93	98	78	93	90	100	96	69	84	86	76	68	76	80	98	100	98	100	100	97	99	100	100	97	100	2	3	3	
7	Rani	40	F	I	BB	101	Appendicectomy	3	3	358	291	252	91	94	74	87	92	45	92	76	89	75	100	89	68	97	63	70	68	72	83	73	62	100	98	99	97	98	99	99	97	99	99	99	100	2	3	2	Bradycardia,
8	Loganathan	34	M	I	BB	105	Hernioplasty	3	3	355	275	298	77	75	94	98	80	62	97	94	74	60	77	70	99	67	90	73	94	87	60	95	66	72	97	98	100	98	97	97	99	100	99	99	99	2	3	3	
9	Neelakandan	45	M	I	BB	117	Hernioplasty	4	3	357	283	299	95	63	92	71	62	61	94	76	96	61	98	74	88	98	59	67	97	72	74	77	99	71	97	99	100	99	98	97	97	99	99	97	97	2	3	3	Hypotension
10	Mohan	39	M	I	BB	110	Appendicectomy	3	5	360	360	292	74	98	63	80	91	86	62	74	66	69	89	89	67	96	75	68	64	78	77	60	81	79	97	98	99	98	97	100	98	97	100	99	100	1	2	2	
11	Mani	36	F	I	BB	105	Hernioplasty	4	4	335	254	287	73	96	65	67	74	93	91	76	77	69	68	84	98	74	78	73	80	69	65	71	76	93	97	98	97	98	97	98	98	99	100	100	97	2	3	2	
12	Tamilvannan	29	M	II	BB	120	Hernioplasty	3	4	352	360	267	79	88	81	44	61	81	86	96	71	68	83	86	87	65	94	92	77	65	68	97	91	93	97	97	97	100	99	98	99	99	97	97	100	1	3	2	Bradycardia,
13	Knadapalam	31	M	I	BB	92	Hernioplasty	4	4	346	341	275	95	78	68	63	76	80	72	61	73	68	76	81	78	94	82	63	80	80	63	73	69	69	100	97	99	100	97	98	98	100	97	98	98	1	2	3	
14	Moorthy	44	M	II	BB	91	Appendicectomy	3	5	309	291	282	75	68	95	87	97	87	95	76	95	68	67	80	95	60	60	99	81	74	95	78	89	78	100	100	97	99	100	100	99	98	99	97	97	2	3	2	
15	Vijaya	60	F	I	BB	113	Hernioplasty	3	3	337	262	269	94	76	84	93	93	62	72	69	65	97	94	93	69	77	75	95	99	79	73	96	70	75	100	100	98	99	100	99	99	97	100	99	98	2	3	3	Vomiting
16	Srinivasan	38	M	I	BB	115	Hernioplasty	3	4	303	300	297	61	74	80	92	68	78	72	62	80	78	78	99	76	60	97	64	95	67	95	90	78	94	97	97	99	98	99	98	100	99	98	97	98	1	2	2	
17	Ponnusamy	43	M	I	BB	100	Appendicectomy	3	3	357	243	260	69	92	82	74	100	86	69	64	66	70	78	65	61	95	62	62	77	96	64	84	78	70	97	100	98	97	99	98	97	98	100	97	98	1	2	3	
18	Ramamoorthy	45	M	II	BB	96	Hernioplasty	4	4	310	331	262	70	97	60	95	46	83	78	98	62	87	60	61	80	53	77	75	92	95	65	60	62	66	99	99	99	97	97	97	97	99	97	99	100	2	2	3	Bradycardia,Hypotension

S No	Name	Age(years)	Sex	ASA	Group	Duration of the surgery (min)	Surgery	Time of onset of Sensory Block(min)	Time of onset of motor Block(min)	Duration of sensory block(min)	Duration of motor block(min)	Time of sensory regression to S1(min)	HR(per min)												Mean arterial pressure (mm of Hg)												SPO2(%)												Sedation score			Adverse effects
													0	3	5	10	15	20	25	30	35	40	45	0	3	5	10	15	20	25	30	35	40	45	0	3	5	10	15	20	25	30	35	40	45	Pre Op	10 min after spinal anaesthesia	Post Op	
19	Sivakami	31	F	II	BB	107	Appendicectomy	3	3	329	288	251	82	67	98	72	85	97	98	92	99	99	87	86	62	67	68	66	63	82	93	63	81	97	97	97	97	97	99	100	98	100	100	100	100	100	2	3	2	Vomiting
20	Chandran	39	M	II	BB	93	Hernioplasty	4	5	338	308	275	95	76	72	78	74	98	66	98	66	80	82	96	83	83	77	66	62	85	73	68	77	60	99	98	98	98	99	98	99	100	98	100	98	2	2	2	Shivering
21	Thirunavukarasu	58	M	I	BB	96	Appendicectomy	3	4	317	332	275	60	98	94	80	98	80	85	94	85	89	63	75	92	67	54	74	92	66	70	92	74	67	100	99	100	100	98	97	100	99	98	99	99	1	3	2	Hypotension
22	Ravi	21	M	II	BB	117	Hernioplasty	3	3	353	317	267	61	93	71	100	98	65	84	80	86	71	95	93	99	60	56	89	92	73	74	70	69	87	100	98	99	99	99	97	99	98	97	97	98	2	2	3	Hypotension
23	Asokan	24	M	II	BB	97	Hernioplasty	4	4	324	257	290	94	77	90	86	90	98	81	68	91	97	91	91	92	60	57	80	93	84	72	96	94	77	97	97	98	99	98	98	98	100	98	98	100	2	3	2	Hypotension
24	Govindaraj	51	M	I	BB	92	Hernioplasty	4	5	304	274	259	92	95	71	70	78	86	68	74	92	84	89	84	94	66	79	88	86	100	89	78	85	70	100	100	99	97	97	98	98	99	97	97	97	1	2	2	Vomiting
25	Rajendran	55	M	I	BB	102	Hernioplasty	4	5	314	266	281	88	98	78	44	84	66	81	89	76	85	79	84	82	78	91	66	61	68	64	98	100	81	97	97	100	100	100	97	98	100	98	98	98	2	2	3	Bradycardia,
26	Kannan	55	M	II	BB	109	Appendicectomy	3	4	324	266	293	61	99	99	79	71	60	67	85	87	67	67	63	64	62	81	59	93	100	66	98	71	83	100	98	99	98	98	98	97	99	100	100	100	1	2	3	Hypotension
27	Vadivel	41	M	II	BB	93	Hernioplasty	3	3	314	322	282	86	73	64	73	66	82	82	95	95	94	61	75	80	73	99	55	96	61	67	99	65	65	97	97	100	98	99	100	97	100	97	100	100	2	3	3	Hypotension
28	Ravichandran	19	M	II	BB	119	Hernioplasty	3	3	343	266	266	63	69	99	72	70	84	67	77	67	85	66	80	61	90	86	67	69	87	63	85	76	66	100	100	97	98	97	100	97	97	97	99	99	1	3	3	Nausea, Vomiting
29	Rajendran	39	M	I	BB	95	Hernioplasty	4	4	331	281	256	87	67	96	86	94	71	94	65	65	76	72	80	74	81	74	91	73	74	90	96	65	99	97	99	99	97	99	99	100	100	98	100	97	2	2	3	Shivering
30	Appadurai	19	M	I	BB	103	Hernioplasty	4	3	308	256	258	88	68	69	73	48	83	68	67	73	100	60	76	97	86	87	79	100	79	71	98	83	74	100	99	97	100	100	100	99	97	100	99	99	1	3	2	Bradycardia,
31	Rajesh	25	M	I	BD	114	Hernioplasty	2	3	518	458	391	99	73	79	78	90	94	83	74	100	70	100	88	69	61	99	88	68	84	71	81	64	94	99	100	100	99	97	99	99	97	98	98	100	3	3	3	
32	Gurumoorthy	51	M	I	BD	111	Appendicectomy	3	4	501	454	406	79	63	79	73	67	97	80	96	86	94	70	65	93	100	99	80	94	98	74	82	61	85	97	97	98	98	100	99	99	99	98	99	99	3	3	3	
33	Jenitha	25	F	I	BD	110	Hernioplasty	3	5	520	413	409	74	84	75	92	94	86	93	86	83	100	86	77	70	67	94	62	87	83	72	96	65	92	99	98	99	97	100	100	100	100	100	99	97	2	3	3	
34	Senthil kumar	40	M	I	BD	90	Hernioplasty	2	4	490	435	391	77	72	100	82	61	93	64	98	65	72	92	81	78	93	64	85	78	62	97	68	73	79	100	100	98	99	98	100	98	98	98	98	98	2	2	3	
35	Selvaraj	52	M	I	BD	105	Hernioplasty	3	3	480	414	394	71	89	89	72	78	78	68	96	88	83	79	90	72	90	95	87	74	66	85	72	87	96	99	99	100	97	99	97	99	100	97	97	98	2	2	2	
36	Rajeshwari	45	F	I	BD	111	Appendicectomy	3	4	488	426	392	73	71	60	99	89	84	89	84	99	83	71	94	80	70	77	96	69	79	97	81	60	66	98	100	98	98	97	100	97	98	100	99	98	2	3	2	

S No	Name	Age(years)	Sex	ASA	Group	Duration of the surgery (min)	Surgery	Time of onset of Sensory Block(min)	Time of onset of motor Block(min)	Duration of sensory block(min)	Duration of motor block(min)	Time of sensory regression to S1(min)	HR(per min)												Mean arterial pressure (mm of Hg)												SPO2(%)												Sedation score			Adverse effects
													0	3	5	10	15	20	25	30	35	40	45	0	3	5	10	15	20	25	30	35	40	45	0	3	5	10	15	20	25	30	35	40	45	Pre Op	10 min after spinal anaesthesia	Post Op	
37	Thangam	37	F	I	BD	116	Hernioplasty	2	4	507	429	394	60	67	90	87	88	81	96	73	79	61	93	78	68	96	75	63	76	73	92	60	72	74	99	97	97	100	100	99	98	98	97	97	98	2	3	2	
38	Narayanan	60	M	I	BD	120	Hernioplasty	3	5	511	431	409	70	67	75	74	61	82	60	65	63	74	61	86	91	73	92	97	98	94	80	87	70	88	98	99	97	97	98	98	97	98	98	98	97	3	3	3	
39	Rajeshkanna	24	M	I	BD	118	Appendicectomy	2	3	516	429	404	65	81	93	82	77	80	72	67	69	79	84	70	85	95	90	84	92	61	69	71	77	66	99	97	97	100	100	99	97	98	97	100	100	2	3	2	
40	Natarajan	60	M	I	BD	115	`	3	4	486	431	395	83	69	64	81	84	67	68	95	89	93	77	77	91	84	60	71	66	88	84	99	64	86	100	100	100	99	98	97	98	100	99	100	97	2	3	3	
41	Subramaniyan	37	M	I	BD	115	Appendicectomy	2	4	505	435	401	72	94	96	61	96	94	74	86	73	80	62	96	97	64	74	90	69	69	62	84	83	61	100	100	100	99	100	97	97	100	98	97	98	3	3	3	
42	Natrajan	49	M	II	BD	101	Hernioplasty	3	4	487	414	405	90	71	93	92	66	74	84	90	89	71	83	95	94	91	81	66	66	74	74	74	75	61	98	99	98	98	100	99	98	100	98	97	98	2	3	2	
43	Aruvambal	45	F	I	BD	104	Hernioplasty	3	4	502	426	391	87	75	81	91	84	70	88	65	87	78	68	67	69	65	89	82	62	82	64	98	65	72	98	100	98	98	97	98	97	100	97	99	98	3	3	2	
44	Robinson	35	M	II	BD	98	Appendicectomy	3	3	518	429	392	68	68	77	85	97	74	84	89	86	100	62	62	76	80	98	64	60	87	64	69	100	66	100	98	97	100	97	99	98	98	98	100	98	3	3	3	
45	Arokiadoss	46	M	I	BD	99	Hernioplasty	2	4	486	431	409	78	63	93	66	73	67	73	65	74	78	75	94	93	75	77	78	87	86	65	92	68	72	99	99	99	97	98	98	99	99	100	97	97	3	3	2	
46	Gandhimathi	55	F	I	BD	96	Hernioplasty	2	3	509	426	403	83	75	69	65	70	45	60	89	82	74	62	71	96	64	78	92	94	72	75	96	93	60	99	98	99	99	98	100	97	100	97	98	98	2	2	3	Bradycardia
47	Sekar	45	M	I	BD	120	Appendicectomy	2	4	507	429	392	67	61	63	89	77	75	67	65	76	61	67	60	89	98	87	74	94	88	64	62	86	87	99	97	97	100	100	98	97	98	99	100	99	2	3	3	
48	Kannadasan	18	M	II	BD	95	Hernioplasty	3	5	484	431	395	79	82	68	85	82	62	96	77	64	93	71	80	60	77	89	64	69	92	70	77	86	62	99	97	97	98	100	100	99	98	97	97	99	2	3	2	
49	Bagyam	60	F	II	BD	111	Hernioplasty	3	3	502	430	391	70	75	85	63	94	90	74	96	60	82	69	89	71	61	65	69	99	65	84	89	69	90	98	97	98	98	98	100	100	100	97	98	100	3	2	3	
50	Muthukumar	38	M	II	BD	90	Appendicectomy	3	3	490	456	395	90	68	74	94	68	94	66	69	85	97	82	71	73	72	93	91	84	95	71	100	91	65	100	98	99	100	100	99	97	100	98	99	98	3	2	2	
51	Sivashankar	41	M	I	BD	112	Hernioplasty	3	5	500	460	404	67	69	78	63	49	97	69	61	84	87	94	87	84	100	73	62	96	73	80	82	88	73	97	99	97	99	99	97	100	97	97	97	99	2	2	3	Bradycardia
52	Gunasundari	24	F	II	BD	113	Hernioplasty	2	4	511	436	398	85	69	87	92	80	97	60	92	64	62	72	78	88	71	63	62	61	82	71	97	76	84	99	98	100	98	97	97	98	100	98	98	99	3	3	2	
53	Ravi	58	M	II	BD	115	Appendicectomy	2	5	500	435	396	79	73	90	98	81	100	84	73	72	76	66	66	86	96	96	67	83	78	68	100	62	72	98	97	99	98	99	99	98	100	97	98	100	3	3	2	
54	Anbalagan	45	M	I	BD	114	Hernioplasty	2	5	509	414	404	86	68	97	95	75	96	90	69	96	63	76	88	71	79	95	88	61	91	92	80	89	84	100	97	97	100	97	98	97	97	99	97	98	2	2	2	

S No	Name	Age(years)	Sex	ASA	Group	Duration of the surgery (min)	Surgery	Time of onset of Sensory Block(min)	Time of onset of motor Block(min)	Duration of sensory block(min)	Duration of motor block(min)	Time of sensory regression to S1(min)	HR(per min)												Mean arterial pressure (mm of Hg)												SPO2(%)												Sedation score			Adverse effects
													0	3	5	10	15	20	25	30	35	40	45	0	3	5	10	15	20	25	30	35	40	45	0	3	5	10	15	20	25	30	35	40	45	Pre Op	10 min after spinal anaesthesia	Post Op	
55	Mohamed raffiq	31	M	I	BD	108	Appendicectomy	3	5	515	426	389	77	92	65	67	60	83	65	68	73	83	60	84	70	75	65	89	82	61	77	85	79	88	100	99	98	100	99	99	99	100	98	99	99	3	3	3	
56	Rajangam	23	M	II	BD	100	Hernioplasty	3	5	511	426	398	83	93	97	63	74	96	95	87	68	79	87	80	96	92	99	64	72	84	95	68	79	76	99	97	100	98	97	100	99	98	100	98	99	3	2	2	
57	Sundaraj	24	M	II	BD	91	Hernioplasty	2	5	488	429	392	92	85	84	73	90	77	97	69	71	78	99	75	77	96	75	98	93	76	86	88	66	60	100	97	100	97	100	99	99	100	98	99	98	2	2	2	
58	Govindaraj	49	M	II	BD	107	Appendicectomy	3	5	519	431	396	75	67	69	86	63	62	92	99	85	95	62	79	87	64	69	87	89	92	61	90	77	78	99	97	100	98	99	100	99	97	98	100	98	3	3	2	
59	Veerapandi	22	M	I	BD	110	Hernioplasty	3	5	513	430	398	78	72	89	71	83	98	72	88	69	91	88	81	81	63	95	69	98	73	98	90	93	90	99	97	97	100	98	100	98	98	97	99	97	2	2	2	
60	Marimuthu	42	M	I	BD	91	Hernioplasty	2	4	491	456	409	66	72	73	91	83	79	94	65	66	85	73	96	72	98	90	100	65	80	67	86	75	100	98	98	100	98	100	100	97	99	99	100	98	3	2	2	